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NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload
NEWS 8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS 9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS 10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS 11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS 12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
NEWS 13	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS 14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS 15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS 16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 17	Oct 22	Over 1 million reactions added to CASREACT
NEWS 18	Oct 22	DGENE GETSIM has been improved
NEWS 19	Oct 29	AAASD no longer available
NEWS 20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS 21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS 22	Nov 29	COPPERLIT now available on STN
NEWS 23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS 24	Nov 30	Files VETU and VETB to have open access
NEWS 25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 26	Dec 10	DGENE BLAST Homology Search
NEWS 27	Dec 17	WELDASEARCH now available on STN
NEWS 28	Dec 17	STANDARDS now available on STN
NEWS 29	Dec 17	New fields for DPCI
NEWS 30	Dec 19	CAS Roles modified
NEWS 31	Dec 19	1907-1946 data and page images added to CA and CAplus

NEWS EXPRESS	August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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=> s bone morphogenetic protein

20 FILES SEARCHED...
L1 15310 BONE MORPHOGENETIC PROTEIN

=> s articular cartilage and regeneration

L2 1060 ARTICULAR CARTILAGE AND REGENERATION

=> s l2 and l1

L3 71 L2 AND L1

=> s l3 and method

L4 31 L3 AND METHOD

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L4 ANSWER 1 OF 31 USPATFULL
TI Methods and articles for regenerating living tissue
AB There are numerous medical situations involving deficiencies of living tissue and where increase of living tissue mass is desired. Methods are described wherein a configured, shell-like device that is capable of being penetrated by living cells and tissues, is implanted into the body of a mammal in such a way as to establish a space, the space being at least partly, bounded by the device. The configuration of the device is such that the configuration of the established space is essentially the same as the configuration of living tissue that is desired for treatment of the tissue deficiency. At least one tissue stimulating molecular substance is placed within the established space for the purpose of stimulating the growth of desired living tissue within the established space. A kit for the generation of desired living tissue, comprised of the components mentioned above, is also disclosed.

ACCESSION NUMBER: 2001:226051 USPATFULL
TITLE: Methods and articles for regenerating living tissue
INVENTOR(S): Hardwick, William R., Flagstaff, AZ, United States
Thomson, Robert C., Flagstaff, AZ, United States
Cleek, Robert L., Flagstaff, AZ, United States

Mane, Shrikant M., Flagstaff, AZ, United States
Cook, Alonzo D., Flagstaff, AZ, United States
PATENT ASSIGNEE(S): [redacted]ore Enterprise Holdings, Inc., [redacted]ewark, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6328765	B1	20011211
APPLICATION INFO.:	US 1998-205521		19981203 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Willse, David H.
ASSISTANT EXAMINER: Stewart, Alvin
LEGAL REPRESENTATIVE: Sheets, Eric J
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 25 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2632

L4 ANSWER 2 OF 31 USPATFULL
TI Pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof
AB The invention is in the area of pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof. In particular, the invention includes isolated adipose tissue derived stromal cells that have been induced to express at least one phenotypic characteristic of a neuronal, astroglial, hematopoietic progenitor, or hepatic cell. The invention also includes an isolated adipocyte tissue-derived stromal cell that has been dedifferentiated such that there is an absence of adipocyte phenotypic markers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:188204 USPATFULL
TITLE: Pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof
INVENTOR(S): Wilkison, William O., Bahama, NC, United States
Gimble, Jeffrey, Chapel Hill, NC, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001033834	A1	20011025
APPLICATION INFO.:	US 2001-793173	A1	20010226 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-185338	20000226 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Sherry M. Knowles, Esq., KING & SPALDING, 45th Floor, 191 Peachtree Street, N.E., Atlanta, GA, 30303
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
LINE COUNT: 1236
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 3 OF 31 USPATFULL
TI Repair of larynx, trachea, and other fibrocartilaginous tissues
AB Provided herein are methods and devices for inducing the formation of functional replacement nonarticular cartilage tissues and ligament tissues. These methods and devices involve the use of osteogenic proteins, and are useful in repairing defects in the larynx, trachea, interarticular menisci, intervertebral discs, ear, nose, ribs and other

fibrocartilaginous tissues in a mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:165613 USPATFULL
TITLE: Repair of larynx, trachea, and other fibrocartilaginous tissues
INVENTOR(S): Vukicevic, Slobodan, Zagreb, Croatia
Katic, Vladimir, Zagreb, Croatia
Sampath, Kuber T., Holliston, MA, United States
PATENT ASSIGNEE(S): Creative BioMolecules, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001024823	A1	20010927
APPLICATION INFO.:	US 2001-828607	A1	20010406 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 1999-US17222, filed on 30 Jul 1999, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-103161	19981006 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & NEAVE, 1251 AVENUE OF THE AMERICAS, 50TH FLOOR, NEW YORK, NY, 10020-1105
NUMBER OF CLAIMS: 56
EXEMPLARY CLAIM: 1
LINE COUNT: 1859
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 4 OF 31 USPATFULL
TI BMP-9 compositions
AB Purified **bone morphogenetic protein**-9 (BMP-9) proteins and processes for producing them are disclosed. The proteins may be used in the treatment of bone and cartilage defects and in wound healing and related tissue repair.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:152724 USPATFULL
TITLE: BMP-9 compositions
INVENTOR(S): Rosen, Vicki A., Brookline, MA, United States
Wozney, John M., Hudson, MA, United States
Celeste, Anthony J., Hudson, MA, United States
Thies, R. Scott, Andover, MA, United States
Song, Jeffrey R., Brookline, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6287816	B1	20010911
APPLICATION INFO.:	US 1994-254353		19940606 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-50132, filed on 22 Apr 1993, now patented, Pat. No. US 5661007 Continuation-in-part of Ser. No. US 1991-720590, filed on 25 Jun 1991, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1992-US5374	19920625

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Romeo, David

LEGAL REPRESENTATIVE: Kapinos, Ellen J.
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 1308
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 5 OF 31 USPATFULL
TI Device and methods for in vivo culturing of diverse tissue cells
AB An anatomically specific, bioresorbable, implant device for facilitating the healing of voids in bone, cartilage and soft tissue is disclosed. A preferred embodiment of using the implant device for facilitating the healing of a human joint lesion includes a cartilage region invested with an alginate microstructure joined with a subchondral bone region invested with a hyaluronan microstructure. The alginate selectively dispersed in the cartilage region enhances the environment for chondrocytes to grow **articular cartilage**. The hyaluronan selectively dispersed in the subchondral bone region enhances the environment for mesenchymal cells which migrate into that region's macrostructure and which differentiate into osteoblasts. The microstructures can be invested at varying concentrations in the regions. A hydrophobic barrier, strategically positioned within the subchondral bone region macrostructure, shields the chondrocytes from the oxygenated blood in subchondral cancellous bone. In the preferred form, the cartilage region includes a tangential zone including a network of intercommunicating void spaces having a horizontal orientation and in communication with synovial fluid and includes a radial zone including multiple void spaces oriented in both horizontal and vertical planes and providing intercommunication between the tangential zone and the subchondral bone region.

ACCESSION NUMBER: 2001:116310 USPATFULL
TITLE: Device and methods for in vivo culturing of diverse tissue cells
INVENTOR(S): Brekke, John H., Duluth, MN, United States
PATENT ASSIGNEE(S): Kensey Nash Corporation, Exton, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6264701	B1	20010724
APPLICATION INFO.:	US 1998-206604		19981207 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-242557, filed on 13 May 1994, now patented, Pat. No. US 5981825
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Milano, Michael J.
LEGAL REPRESENTATIVE: Kamrath, Alan D.Rider Bennett Egan & Arundel LLP
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1148

L4 ANSWER 6 OF 31 USPATFULL
TI Methods for accelerating bone and cartilage growth and repair
AB The present invention provides improved methods, kits, and compositions for enhancing bone, cartilage and cartilage repair, bone and prosthesis implantation, and attachment and fixation of cartilage and cartilage to bone or other tissues, and chondrocyte proliferation comprising the administration of an effective amount of angiotensinogen, angiotensin I (AI), AI analogues, AI fragments and analogues thereof, angiotensin II

(AII), AII analogues, AII fragments or analogues thereof or AII AT.sub.2
type 2 receptor agonists.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:107861 USPATFULL
TITLE:	Methods for accelerating bone and cartilage growth and repair
INVENTOR(S):	Rodgers, Kathleen E., Long Beach, CA, United States DiZerega, Gere S., Pasedena, CA, United States
PATENT ASSIGNEE(S):	University of Southern California, Los Angeles, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6258778	B1	20010710	
APPLICATION INFO.:	US 1999-352191		19990712	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-92653	19980713	(60)
	US 1999-130855	19990422	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Davenport, Avis M.
LEGAL REPRESENTATIVE:	McDonnell, Boehnen, Hulbert & Berghoff, Harper, David S.
NUMBER OF CLAIMS:	35
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT:	1595

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 7 OF 31 USPATFULL

TI Condensed 4,5,6,7-tetrahydrobenzo[C]thiophenes as enhancer for cell differentiation induction factor action

AB A compound represented by the formula: ##STR1##

wherein X represents a sulfur atom or an oxygen atom; Y represents an optionally oxidized sulfur atom or an oxygen atom; Z represents a bond or a divalent hydrocarbon group; R.sup.1 represents an optionally substituted hydrocarbon group; R.sup.2 represents an optionally amidated
or esterified carboxyl group; ring A represents an optionally substituted aromatic 5-membered heterocyclic ring; or a salt thereof.

A compound of the above formula possesses cell differentiation inducing factor action-enhancing activity and anti-matrix metalloprotease activity and that is useful in the prevention and treatment of bone diseases such as osteoporosis, bone fractures, osteoarthritis and rheumatoid arthritis, arteriosclerosis, cancer metastasis, and diseases based on nerve degeneration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2001:82796 USPATFULL
TITLE:	Condensed 4,5,6,7-tetrahydrobenzo[C]thiophenes as enhancer for cell differentiation induction factor action
INVENTOR(S):	Yasuma, Tsuneo, Ibaraki, Japan Oda, Tsuneo, Ibaraki, Japan Hazama, Masatoshi, Ikeda, Japan Taketomi, Shigehisa, Ikeda, Japan
PATENT ASSIGNEE(S):	Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6242471	B1	20010605
APPLICATION INFO.:	US 2000-559453		20000428 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-252913, filed on 19 Feb 1999, now patented, Pat. No. US 6066658 Continuation of Ser. No. WO 1997-JP3122, filed on 5 Sep 1997		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1996-237006	19960906

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Stockton, Laura L.
LEGAL REPRESENTATIVE: Fitzpatrick, Cella, Harper & Scinto
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 2656
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 8 OF 31 USPATFULL

TI Aldehyde and glycosidase-treated soft and bone tissue xenografts

AB The invention provides articles of manufacture comprising substantially non-immunogenic soft and bone tissue xenografts for implantation into humans. The invention further provides methods for preparing soft and bone tissue xenografts by removing at least a portion of a soft or bone tissue from a non-human animal to provide a xenograft; washing the xenograft in saline and alcohol; subjecting the xenograft to cellular disruption treatment; exposing the xenograft to an aldehyde in an amount ranging from about 0.01% to about 0.10%; and digesting the xenograft with a glycosidase and optionally following with a capping treatment. The invention also provides an article of manufacture produced by the above-identified **method** of the invention. The invention further provides a soft or bone tissue xenograft for implantation into a human including a portion of a soft or bone tissue from a non-human animal, wherein the portion has extracellular components and substantially only dead cells. The extracellular components have substantially no surface carbohydrate moieties which are susceptible to glycosidase digestion. The extracellular components also have an aldehyde in an amount ranging from about 0.01% to about 0.10% crosslinking the proteins of the extracellular components. Each of the xenografts of the invention are substantially non-immunogenic and have substantially the same mechanical properties as a corresponding native soft or bone tissue.

ACCESSION NUMBER: 2001:70845 USPATFULL
TITLE: Aldehyde and glycosidase-treated soft and bone tissue xenografts
INVENTOR(S): Stone, Kevin R., Mill Valley, CA, United States
PATENT ASSIGNEE(S): Crosscart, Inc., Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6231608	B1	20010515
APPLICATION INFO.:	US 1999-248476		19990211 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1998-36171, filed on 6 Mar 1998, now patented, Pat. No. US 5984858 Continuation-in-part of Ser. No. US 1995-483256, filed		

on 7 Jun 1995, now patented, Pat. No. US 5865849
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Isabella, David J.
LEGAL REPRESENTATIVE: McDermott, Will & Emery
NUMBER OF CLAIMS: 59
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 2004

L4 ANSWER 9 OF 31 USPATFULL
TI Biomatrix for soft tissue **regeneration** using mesenchymal stem cells
AB An implant for repair of a tissue defect comprises a plurality of physiologically compatible load-bearing sutures for securing under tension tissue adjacent to the defect to be repaired, the sutures for supporting a tissue reparative cell mass in the defect and a tissue reparative cell mass supported thereby. The sutures have a central portion encapsulated in a cell containing matrix which is contracted under a tensile load by the cells thereof and formed into a mat sheet during the contraction. Spring metal wires hold the sutures in tension during the contraction. The matrix is a collagen gel or other material which the cells contract, the cells comprising human mesenchymal stem cells. The mat sheet is then rolled into a spiral roll with the sutures extending from opposite roll ends to form the desired implant. Different embodiments are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2001:7502 USPATFULL
TITLE: Biomatrix for soft tissue **regeneration** using mesenchymal stem cells
INVENTOR(S): Kadiyala, Sudhakar, Baltimore, MD, United States
Caplan, Arnold I., Cleveland Heights, OH, United States
Fink, David J., Shaker Heights, OH, United States
Young, Randall G., Ellicott City, MD, United States
PATENT ASSIGNEE(S): Osiris Therapeutics, Inc., Baltimore, MD, United States (U.S. corporation)
Case Western Reserve University, Cleveland, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6174333	B1	20010116
APPLICATION INFO.:	US 1998-222688		19981229 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-723260, filed on 30 Sep 1996, now patented, Pat. No. US 5855619
Continuation-in-part of Ser. No. US 1994-254125, filed on 6 Jun 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Isabella, David J.
LEGAL REPRESENTATIVE: Carella, Byrne, et al., Olstein, Elliot M., Squire, William
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1016
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 10 OF 31 USPATFULL
TI Genetic engineering of cells to enhance healing and tissue

regeneration

AB A **method** for en[redacted]cing and/or increasing the effi[redacted]ency of repair of tissue, primarily bone or cartilage, [redacted]ng genetically engineered cells has been developed. In the preferred embodiment, mesenchymal stem cells are isolated from periosteum tissue, and transfected with the gene encoding a growth factor for the particular cell type to be repaired. For example, for repair of bone, a gene (or genes) encoding bone morphogenic protein is transfected into periosteal cells. The transfected periosteal cells then express the bone morphogenic protein in culture to promote bone repair as a function of the expressed bone morphogenic protein. Cells can be transfected using any appropriate means, including viral vectors, as shown by the example, chemical transfectants, or physico-mechanical methods such as electroporation and direct diffusion of DNA. Genes can encode any useful protein, for example, a specific growth factor, morphogenesis factor, a structural protein, or a cytokine which enhances the temporal sequence of wound repair, alters the rate of proliferation, increases the metabolic synthesis of extracellular matrix proteins, or directs phenotypic expression in endogenous cell populations. Representative genes encoding proteins include bone growth factor genes, cartilage growth factor genes, nerve growth factor genes, and general growth factors important in wound healing, such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF-1), epidermal growth factor (EGF), basic fibroblast growth factor (FGF), endothelial derived growth supplement.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2000:77502 USPATFULL
TITLE: Genetic engineering of cells to enhance healing and tissue **regeneration**
INVENTOR(S): Breitbart, Arnold S., Great Neck, NY, United States
Grande, Daniel S., Sea Cliff, NY, United States
Mason, James M., Bethpage, NY, United States
PATENT ASSIGNEE(S): North Shore-Long Island Jewish Research Institute, Manhasset, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6077987		20000620	
APPLICATION INFO.:	US 1997-923718		19970904	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Yu, Mickey
ASSISTANT EXAMINER: Nguyen, Tram A.
LEGAL REPRESENTATIVE: Arnall Golden & Gregory, LLP
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 955
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 11 OF 31 USPATFULL

TI Recombinant production of latent TGF-beta binding protein-3 (LTBP-3)

AB Disclosed are novel nucleic acid and peptide compositions comprising latent TGF.beta. binding proteins (LTBPs). Also disclosed are methods of using LTBP-2 and LTBP-3 peptides and the DNA segments which encode them.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2000:74106 USPATFULL
TITLE: Recombinant production of latent TGF-beta binding protein-3 (LTBP-3)

INVENTOR(S): Bonadio, Jeffrey, Ann Arbor, MI, United States
[redacted]in, Wushan, Ann Arbor, MI, Unit[redacted] States
PATENT ASSIGNEE(S): [redacted]he Regents of The University o[redacted]ichigan, Ann Arbor, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6074840		20000613
APPLICATION INFO.:	US 1995-479722		19950607 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1995-US2251, filed on 21 Feb 1995 which is a continuation-in-part of Ser. No. US 1994-316650, filed on 30 Sep 1994, now patented,
Pat. No. US 5942496 which is a continuation-in-part of Ser. No. US 1994-199780, filed on 18 Feb 1994, now patented, Pat. No. US 5763416

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fitzgerald, David L.
LEGAL REPRESENTATIVE: William, Morgan & Amerson
NUMBER OF CLAIMS: 43
EXEMPLARY CLAIM: 1,20
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 4758
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 12 OF 31 USPATFULL
TI Condensed 4,5,6,7-tetrahydrobenzo[C]thiophenes as enhancer for cell differentiation induction factor action
AB A compound represented by the formula: ##STR1## wherein X represents a sulfur atom or an oxygen atom; Y represents an optionally oxidized sulfur atom or an oxygen atom; Z represents a bond or a divalent hydrocarbon group; R.sup.1 represents an optionally substituted hydrocarbon group; R.sup.2 represents an optionally amidated or esterified carboxyl group; ring A represents an optionally substituted aromatic 5-membered heterocyclic ring; or a salt thereof. A compound of the above formula possesses cell differentiation inducing factor action-enhancing activity and anti-matrix metalloprotease activity and that is useful in the prevention and treatment of bone diseases such as osteoporosis, bone fractures, osteoarthritis and rheumatoid arthritis, arteriosclerosis, cancer metastasis, and diseases based on nerve degeneration.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:64884 USPATFULL
TITLE: Condensed 4,5,6,7-tetrahydrobenzo[C]thiophenes as enhancer for cell differentiation induction factor action
INVENTOR(S): Yasuma, Tsuneo, Ibaraki, Japan
Oda, Tsuneo, Ibaraki, Japan
Hazama, Masatoshi, Ikeda, Japan
Taketomi, Shigehisa, Ikeda, Japan
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6066658		20000523
APPLICATION INFO.:	US 1999-252913		19990219 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 1997-JP3122, filed on 5 Sep
1997

	NUMBER	DATE

PRIORITY INFORMATION:	JP 1996-237006 19960906
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Stockton, Laura L.
LEGAL REPRESENTATIVE:	Fitzpatrick, Cella, Harper & Scinto
NUMBER OF CLAIMS:	18
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:	2644

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 13 OF 31 USPATFULL

TI **Bone morphogenetic protein** (BMP)-9 compositions and their uses

AB Purified **Bone Morphogenetic Protein** (BMP)-9 proteins and processes for producing them are disclosed. The proteins may be used in the treatment of bone and cartilage defects and in wound healing and related tissue repair, and in hepatic growth and function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2000:27958 USPATFULL
TITLE:	**Bone morphogenetic protein** (BMP)-9 compositions and their uses
INVENTOR(S):	Thies, R. Scott, Andover, MA, United States Song, Jeffrey J., Brighton, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6034062		20000307
APPLICATION INFO.:	US 1997-815652		19970313 (8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Kemmerer, Elizabeth
ASSISTANT EXAMINER:	Romeo, David S.
LEGAL REPRESENTATIVE:	Mienert, M. C., Kapinos, Ellen J.
NUMBER OF CLAIMS:	3
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT:	2197

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 14 OF 31 USPATFULL

TI BMP-9 compositions

AB Purified **Bone Morphogenetic Protein** (BMP)-9 proteins and processes for producing them are disclosed. The proteins may be used in the treatment of bone and cartilage defects and in wound healing and related tissue repair, and in hepatic growth and function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2000:27957 USPATFULL
TITLE:	BMP-9 compositions
INVENTOR(S):	Rosen, Vicki A., Chestnut Hill, MA, United States Wozney, John M., Hudson, MA, United States Celeste, Anthony J., Hudson, MA, United States Thies, Scott R., Andover, MA, United States Song, Jeffrey R., Brookline, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6034061		20000307
APPLICATION INFO.:	US 1996-750222		19961204 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-254353, filed on 6 Jun
1994 which is a continuation of Ser. No. US 1993-50132,
filed on 22 Apr 1993, now patented, Pat. No. US 5661007
which is a continuation-in-part of Ser. No. WO 1992-US5374, filed on 25 Jun 1992 which is a continuation-in-part of Ser. No. US 1991-720590, filed on 25 Jun 1991, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kemmerer, Elizabeth C
ASSISTANT EXAMINER: Romeo, David S.
LEGAL REPRESENTATIVE: Kapinos, Ellen J.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 19 Drawing Page(s)
LINE COUNT: 1851
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 31 USPATFULL
TI Continuous release polymeric implant carrier
AB Biodegradable, porous, polymeric implant material provides substantially
continuous release of bioactive agent during in vivo use. Bioactive agent is initially released in amounts that are less than degradation rate of polymer, thereby promoting migration of cells into material. Later larger amounts of bioactive agent is released, thereby promoting differentiation of cells. **Method** of making material includes step of applying vacuum to form pores. Implant material may be adapted for one phase implant (e.g., for bone or cartilage) or for two phase layered implant (e.g., for cartilage layer on top of bone layer).

ACCESSION NUMBER: 2000:5014 USPATFULL
TITLE: Continuous release polymeric implant carrier
INVENTOR(S): Athanasiou, Kyriacos A, San Antonio, TX, United States
Boyan, Barbara D, San Antonio, TX, United States
PATENT ASSIGNEE(S): The University of Texas System, Austin, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6013853		20000111
APPLICATION INFO.:	US 1994-196970		19940215 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-123812, filed on 20 Sep 1993, now patented, Pat. No. US 5607474 which
is a continuation of Ser. No. US 1992-837401, filed on 14 Feb 1992, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Isabella, David
LEGAL REPRESENTATIVE: Greenlee, Winner and Sullivan, P.C.
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1602

L4 ANSWER 16 OF 31 USPATFULL

TI Device and methods for in vivo culturing of diverse tissue cells
AB An anatomically specific, bioresorbable, implant device for facilitating
the healing of voids in bone, cartilage and soft tissue is disclosed. A preferred embodiment of using the implant device for facilitating the healing of a human joint lesion includes a cartilage region invested with an alginate microstructure joined with a subchondral bone region invested with a hyaluronan microstructure. The alginate selectively dispersed in the cartilage region enhances the environment for chondrocytes to grow **articular cartilage**. The
hyaluronan selectively dispersed in the subchondral bone region enhances
the environment for mesenchymal cells which migrate into that region's macrostructure and which differentiate into osteoblasts. The microstructures can be invested at varying concentrations in the regions. A hydrophobic barrier, strategically positioned within the subchondral bone region macrostructure, shields the chondrocytes from the oxygenated blood in subchondral cancellous bone. In the preferred form, the cartilage region includes a tangential zone including a network of intercommunicating void spaces having a horizontal orientation and in communication with synovial fluid and includes a radial zone including multiple void spaces oriented in both horizontal and vertical planes and providing intercommunication between the tangential zone and the subchondral bone region.

ACCESSION NUMBER:	1999:142232 USPATFULL
TITLE:	Device and methods for in vivo culturing of diverse tissue cells
INVENTOR(S):	Brekke, John H., Duluth, MN, United States
PATENT ASSIGNEE(S):	THM Biomedical, Inc., Duluth, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5981825		19991109
APPLICATION INFO.:	US 1994-242557		19940513 (8)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Clarke, Robert A.
LEGAL REPRESENTATIVE:	Kamrath, AlanPeterson, Wicks, Nemer & Kamrath, P.A.
NUMBER OF CLAIMS:	42
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	9 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	1250

L4 ANSWER 17 OF 31 USPATFULL
TI Collagen-polysaccharide matrix for bone and cartilage repair
AB A matrix and a **method** for preparing it are provided to support the growth of tissue, such as bone, cartilage or soft tissue. A polysaccharide is reacted with an oxidizing agent to open sugar rings on
the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to collagen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	1999:132276 USPATFULL
TITLE:	Collagen-polysaccharide matrix for bone and cartilage repair
INVENTOR(S):	Liu, LinShu, Sunnyvale, CA, United States Spiro, Robert, Half Moon Bay, CA, United States
PATENT ASSIGNEE(S):	Orquest, Inc., Mountain View, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5972385		19991026
APPLICATION INFO.:	US 1998-7731		1998011[redacted](9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-783650, filed on 15 Jan 1997, now patented, Pat. No. US 5866165
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Webman, Edward J.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 948
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 18 OF 31 USPATFULL
TI Methods and compositions for multiple gene transfer into bone cells
AB Disclosed are methods, compositions, kits and devices for use in transferring nucleic acids into bone cells in situ and/or for stimulating bone progenitor cells. Type II collagen and, particularly, osteotropic genes, are shown to stimulate bone progenitor cells and to promote bone growth, repair and **regeneration** in vivo. Gene transfer protocols are disclosed for use in transferring various nucleic acid materials into bone, as may be used in treating various bone-related diseases and defects including fractures, osteoporosis, osteogenesis imperfecta and in connection with bone implants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1999:99644 USPATFULL
TITLE: Methods and compositions for multiple gene transfer into bone cells
INVENTOR(S): Bonadio, Jeffrey, Ann Harbor, MI, United States
Goldstein, Steven A., Ann Harbor, MI, United States
PATENT ASSIGNEE(S): The Regent of The University of Michigan, Ann Arbor, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5942496		19990824
APPLICATION INFO.:	US 1994-316650		19940930 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-199780, filed on 18 Feb 1994, now patented, Pat. No. US 5763416
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Campell, Bruce R.
ASSISTANT EXAMINER: Nguyen, Dave Trong
LEGAL REPRESENTATIVE: Arnold White & Durkee
NUMBER OF CLAIMS: 130
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 5310
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 19 OF 31 USPATFULL
TI Materials and **method** for the immobilization of bioactive species onto biodegradable polymers
AB The present invention is directed to hydrophobic biodegradable polymeric materials having at least one surface thereof rendered more hydrophilic by attachment of at least one layer of a hydrophilic polymer thereto. The hydrophilic polymer layer is cross-linked together on the surface of the biodegradable material with a cross-linking agent or scheme that is biodegradable. Bioactive species are immobilized to chemically

functional groups of the components of the first layer or to unreacted chemically functional groups of the cross-linking agent. Optionally, the bioactive species may be reversibly immobilized through chemically functional linkages that are degradable. The result is an implantable construction with immobilized bioactive species having structural components that are all subject to degradation in the body of a recipient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	1999:72280 USPATFULL
TITLE:	Materials and **method** for the immobilization of bioactive species onto biodegradable polymers
INVENTOR(S):	Cook, Alonzo D., Flagstaff, AZ, United States Drumheller, Paul D., Flagstaff, AZ, United States
PATENT ASSIGNEE(S):	Gore Enterprise Holdings, Inc., Newark, DE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5916585		19990629
APPLICATION INFO.:	US 1997-865800		19970530 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-657083, filed on 3 Jun 1996, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Azpuru, Carlos		
LEGAL REPRESENTATIVE:	Sheets, Eric J		
NUMBER OF CLAIMS:	75		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 3 Drawing Page(s)		
LINE COUNT:	1906		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 20 OF 31 USPATFULL

TI Cartilage induction by bone morphogenetic proteins

AB Compositions of proteins with cartilaginous tissue inducing and maintenance activity are disclosed. The compositions are useful in the treatment of osteoarthritis, cartilage defects and in related tissue repair.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	1999:56457 USPATFULL
TITLE:	Cartilage induction by bone morphogenetic proteins
INVENTOR(S):	Hattersley, Gary, Cambridge, MA, United States Wolfman, Neil M., Dover, MA, United States Morris, Elisabeth A., Southboro, MA, United States Rosen, Vicki A., Chestnut Hill, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5902785		19990511
APPLICATION INFO.:	US 1996-646193		19960507 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-467110, filed on 6 Jun 1995, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Kemmerer, Elizabeth		
LEGAL REPRESENTATIVE:	Lazar, Steven R., Gyure, Barbara A.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
LINE COUNT:	811		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 21 OF 31 USPATFULL
TI Biodegradable implant
AB Biodegradable, porous, polymeric implant material provides substantially
continuous release of bioactive agent during in vivo use. Bioactive agent is initially released in amounts that are less than degradation rate of polymer, thereby promoting migration of cells into material. Later larger amounts of bioactive agent are released, thereby promoting differentiation of cells. **Method** of making material includes steps of applying vacuum temperature and consession to form pores. Implant material may be adapted for one phase implant (e.g., for bone or
cartilage) or for two phase layered implant (e.g., for cartilage layer on top of bone layer).

ACCESSION NUMBER:	1999:26924 USPATFULL		
TITLE:	Biodegradable implant		
INVENTOR(S):	Athanasiou, Kyriacos A., San Antonio, TX, United States		
	Boyan, Barbara D., San Antonio, TX, United States		
PATENT ASSIGNEE(S):	Board of Regents, University of Texas System, Austin, TX, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5876452		19990302
APPLICATION INFO.:	US 1995-452796		19950530 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1994-196970, filed on 15 Feb 1994 which is a continuation-in-part of Ser. No. US 1993-123812, filed on 20 Sep 1993, now patented, Pat. No. US 5607474 which is a continuation of Ser. No. US 1992-837401, filed on 14 Feb 1992, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Isabella, David		
LEGAL REPRESENTATIVE:	Greenlee, Winner and Sullivan, P.C.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)		
LINE COUNT:	1494		

L4 ANSWER 22 OF 31 USPATFULL
TI Biomatrix for soft tissue **regeneration**
AB An implant for repair of a tissue defect which implant comprises a physiologically compatible load-bearing member having an element for securing under tension tissue adjacent to the defect to be repaired, an element for supporting a tissue reparative cell mass in the defect and a
tissue reparative cell mass supported thereby. The implant can be a suture material having a cell containing matrix surrounding a central portion thereof. The matrix is preferably a gel or other material which the cells cause to contract, thereby drawing together the tissues surrounding the defect to which the implant is attached.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	1999:962 USPATFULL
TITLE:	Biomatrix for soft tissue **regeneration**
INVENTOR(S):	Caplan, Arnold I., Cleveland Heights, OH, United States
	Fink, David J., Shaker Heights, OH, United States
	Young, Randell G., Ellicott City, MD, United States
PATENT ASSIGNEE(S):	Case Western Reserve University, Cleveland, OH, United

States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5855619		19990105
APPLICATION INFO.:	US 1996-723360		19960930 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-254125, filed on 6 Jun 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Prebilic, Paul B.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 798
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 23 OF 31 USPATFULL
TI Device and methods for in vivo culturing of diverse tissue cells
AB An anatomically specific, bioresorbable, implant device for facilitating the healing of voids in bone, cartilage and soft tissue is disclosed. A preferred embodiment of using the implant device for facilitating the healing of a human joint lesion includes a cartilage region invested with an alginate microstructure joined with a subchondral bone region invested with a hyaluronan microstructure. The alginate selectively dispersed in the cartilage region enhances the environment for chondrocytes to grow **articular cartilage**. The hyaluronan selectively dispersed in the subchondral bone region enhances the environment for mesenchymal cells which migrate into that region's macrostructure and which differentiate into osteoblasts. The microstructures can be invested at varying concentrations in the regions. A hydrophobic barrier, strategically positioned within the subchondral bone region macrostructure, shields the chondrocytes from the oxygenated blood in subchondral cancellous bone. In the preferred form, the cartilage region includes a tangential zone including a network of intercommunicating void spaces having a horizontal orientation and in communication with synovial fluid and includes a radial zone including multiple void spaces oriented in both horizontal and vertical planes and providing intercommunication between the tangential zone and the subchondral bone region.

ACCESSION NUMBER: 1999:952 USPATFULL
TITLE: Device and methods for in vivo culturing of diverse tissue cells
INVENTOR(S): Brekke, John H., Duluth, MN, United States
Ringeisen, Timothy, Duluth, MN, United States
PATENT ASSIGNEE(S): THM Biomedical, Inc., Duluth, MN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5855608		19990105
APPLICATION INFO.:	US 1994-367510		19941230 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-242557, filed on 13 May 1994
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Clarke, Robert A.
LEGAL REPRESENTATIVE: Peterson, Wicks, Nemer & Kamrath, P.A.
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 1257

L4 ANSWER 24 OF 31 USPATFULL
TI Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide and methods of inducing cartilage by administration of same
AB Compositions of proteins with chondrocyte and cartilaginous tissue inducing activity, as well as **method** of using those compositions, are disclosed. The compositions comprise one or more proteins of the transforming growth factor-.beta. (TGF-.beta.) superfamily of proteins, particularly bone morphogenetic proteins (BMPs), in combination with parathyroid hormone related polypeptide (PTHrP) or an equivalent PTH-like polypeptide. The compositions and methods are useful in the treatment of osteoarthritis, cartilage defects and in related tissue repair.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:154240 USPATFULL
TITLE: Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide and methods of inducing cartilage by administration of same
INVENTOR(S): Hattersley, Gary, 10 Rogers St., #303, Cambridge, MA, United States 02142
Rosen, Vicki A., 2 Cedar Rd., Chestnut Hill, MA, United States 02167

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5846931		19981208
APPLICATION INFO.:	US 1997-926942		19970910 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-622101, filed on 26 Mar 1996, now patented, Pat. No. US 5700774
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kemmerer, Elizabeth
LEGAL REPRESENTATIVE: Lazar, Steven R.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 637
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 25 OF 31 USPATFULL
TI Hand implant device
AB A hand augmentation device to be used to replace diseased tissue of a hand bone. The device includes a dry matrix, which contains at least 75% by weight biocompatible and bioresorbable biopolymeric fibers such as collagen fibers or polysaccharide fibers, and has a height of 2 mm to 4 cm, a width of 0.5 cm to 6 cm, a depth of 0.5 cm to 6 cm, a density of 0.1 g/cm.sup.3 to 0.5 g/cm.sup.3, and a pore size of 50 .mu.m to 300 .mu.m.

ACCESSION NUMBER: 1998:36124 USPATFULL
TITLE: Hand implant device
INVENTOR(S): Li, Shu-Tung, Oakland, NJ, United States
McCarthy, Jack A., Omaha, NE, United States
Rodkey, William G., Edwards, CO, United States
Steadman, J. Richard, Vail, CO, United States
PATENT ASSIGNEE(S): ReGen Biologics, Inc., Redwood City, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5735902		19980407
APPLICATION INFO.:	US 1996-735891		19961023 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-232743, filed on 25 Apr 1994, now patented, Pat. No. US 5624463 which is a continuation-in-part of Ser. No. US 1991-809003, filed on 17 Dec 1991, now patented, Pat. No. US 5306311 which is a continuation-in-part of Ser. No. US 1990-520027, filed on 7 May 1990, now patented, Pat. No. US 5108438 which is a continuation-in-part of Ser. No. US 1989-317951, filed on 2 Mar 1989, now patented, Pat. No. US 5007934 which is a continuation-in-part of Ser. No. US 1987-75352, filed on 20 Jul 1987, now patented, Pat. No. US 5880429

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Isabella, David
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 501

L4 ANSWER 26 OF 31 USPATFULL

TI Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide, and methods of inducing cartilage by administration of same

AB Compositions of proteins with chondrocyte and cartilaginous tissue inducing activity, as well as **method** of using those compositions, are disclosed. The compositions comprise one or more proteins of the transforming growth factor-beta (TGF-beta) superfamily of proteins, particularly bone morphogenetic proteins (BMPs), in combination with parathyroid hormone related polypeptide (PTHrP) or an equivalent PTH-like polypeptide. The compositions and methods are useful in the treatment of osteoarthritis, cartilage defects and in related tissue repair.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 97:120591 USPATFULL
TITLE: Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide, and methods of inducing cartilage by administration of same
INVENTOR(S): Hattersley, Gary, Cambridge, MA, United States
Rosen, Vicki A., Chestnut Hill, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5700774		19971223
APPLICATION INFO.:	US 1996-622101		19960326 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fitzgerald, David L.
ASSISTANT EXAMINER: Kemmerer, Elizabeth C.
LEGAL REPRESENTATIVE: Meinert, M. C., Lazar, S.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 668

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 27 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
TI Device for repairing skeletal joint defect in mammals comprises exogenous osteogenic protein deposited on the surface of a matrix comprising plural distinct tissues derived from proximal or distal hemi-joint.
AN 2000-571418 [53] WPIDS
CR 1996-039987 [04]; 2000-222942 [19]
AB US 6110482 A UPAB: 20001023
NOVELTY - A device (I) for repairing a skeletal joint (SJ) defect in mammals comprising exogenous osteogenic protein deposited on the surface of a biocompatible, biodegradable matrix comprising distinct tissues derived from a proximal or distal hemi-joint including a non-mineralized tissue of a joint and bone underlying the articular surface, is new.

DETAILED DESCRIPTION - (I) serves as a template to form an in vivo functional SJ replacement which is long term mechanically and functionally viable. The matrix defines a unitary intact structure allowing the attachment of infiltrating cells. The underlying bone extends through the margin of **articular cartilage** into the supporting cancellous bone of the proximal or distal hemi-joint, and has dimensions and shape conforming to the SJ to be repaired. The exogenous osteogenic protein is deposited on the matrix surface to induce formation of new distinct tissues, and to permit **regeneration** of a functional SJ replacement comprising distinct tissues.

INDEPENDENT CLAIMS are also included for the following:

(1) a **method** for inducing the formation of a replacement skeletal joint which is mechanically and functionally viable by implanting the above device into a mammal;

(2) a **method** for repairing, in vivo, an **articular cartilage** defect; and

(3) a **method** for repairing, in vivo, a non-mineralized tissue defect in a skeletal joint.

ACTIVITY - Osteopathic.

MECHANISM OF ACTION - Implant.

USE - (I) is useful for inducing the formation of a functional SJ replacement by implanting (I) at a locus in a mammal, and for repairing an **articular cartilage** defect occurring in a synovial cavity in a mammal (claimed). (I) is useful for repair and **regeneration** of distinct tissues at a single defect side in a mammal and for the manufacture, in vivo, of autogenous replacement body parts comprising distinct tissues. (I) serves as a template to form a functional replacement SJ which is long term mechanically and functionally viable.

ADVANTAGE - A cartilage defect in an articulating joint, particularly a superficial **articular cartilage** defect can be functionally restored and the undesirable formation of fibrocartilage as in conventional methods, or degeneration into a full-thickness defect can be avoided. (I) induces formation of bona fide hyaline cartilage rather than fibrocartilage at a defect site.

Dwg.0/4

ACCESSION NUMBER: 2000-571418 [53] WPIDS
CROSS REFERENCE: 1996-039987 [04]; 2000-222942 [19]
DOC. NO. NON-CPI: N2000-422681
DOC. NO. CPI: C2000-170290
TITLE: Device for repairing skeletal joint defect in mammals comprises exogenous osteogenic protein deposited on the surface of a matrix comprising plural distinct tissues derived from proximal or distal hemi-joint.
DERWENT CLASS: A96 B04 D22 P32

INVENTOR(S): KHOURI, R K; RUEGER, D C; SAMPATH, K T
PATENT ASSIGNEE(S): (STRYC) STRYKER CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6110482	A	20000829	(200053)*		21

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6110482	A	CIP of	US 1994-253398	19940603
			US 1995-459129	19950602

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6110482	A	CIP of	US 5906827

PRIORITY APPLN. INFO: US 1995-459129 19950602; US 1994-253398 19940603

L4 ANSWER 28 OF 31 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
AN 2000-514778 [46] WPIDS
AB WO 200044413 A UPAB: 20000921
NOVELTY - **Regeneration** of **articular cartilage** comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein (BMP).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition for **regeneration** of **articular cartilage** comprising at least one BMP.
USE - For regenerating **articular cartilage** injury or defect. The **method** can also be used for the treatment of osteoarthritis which will delay or reduce the need for artificial hip replacements.
ADVANTAGE - This new **method** provides effective repair of articulate cartilage defects and injuries without the need to collect autologous tissue from the patient. Current therapeutic strategies are based on grafting chondral and osteochondral tissues. However, donor tissue is limited and requires surgery at a second site to harvest tissue for implant. As the BMP's can be produced by recombinant DNA technology they are of unlimited supply.
Dwg.0/0
ACCESSION NUMBER: 2000-514778 [46] WPIDS
DOC. NO. NON-CPI: N2000-380459
DOC. NO. CPI: C2000-153579
TITLE: **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
DERWENT CLASS: B04 P34
INVENTOR(S): MORRIS, E; PELUSO, D; ZHANG, R
PATENT ASSIGNEE(S): (GEMY) GENETICS INST INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044413	A1	20000803	(200046)*	EN	17

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000027483	A	20000818	(200057)	
NO 2001003744	A	20010918	(200169)	
EP 1148897	A1	20011031	(200172)	EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

BR 2000007892	A	20011030	(200173)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000044413	A1	WO 2000-US2430	20000131
AU 2000027483	A	AU 2000-27483	20000131
NO 2001003744	A	WO 2000-US2430	20000131
		NO 2001-3744	20010731
EP 1148897	A1	EP 2000-905869	20000131
		WO 2000-US2430	20000131
BR 2000007892	A	BR 2000-7892	20000131
		WO 2000-US2430	20000131

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000027483	A	Based on	WO 200044413
EP 1148897	A1	Based on	WO 200044413
BR 2000007892	A	Based on	WO 200044413

PRIORITY APPLN. INFO: US 2000-493543 20000128; US 1999-118160P 19990201

L4 ANSWER 29 OF 31 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

TI Device for repairing skeletal joint defect in mammals comprises exogenous osteogenic protein deposited on the surface of a matrix comprising plural distinct tissues derived from proximal or distal hemi-joint.

AN 2000-571418 [53] WPIX

CR 1996-039987 [04]; 2000-222942 [19].

AB US 6110482 A UPAB: 20001023

NOVELTY - A device (I) for repairing a skeletal joint (SJ) defect in mammals comprising exogenous osteogenic protein deposited on the surface of a biocompatible, biodegradable matrix comprising distinct tissues derived from a proximal or distal hemi-joint including a non-mineralized tissue of a joint and bone underlying the articular surface, is new.

DETAILED DESCRIPTION - (I) serves as a template to form an in vivo functional SJ replacement which is long term mechanically and functionally viable. The matrix defines a unitary intact structure allowing the attachment of infiltrating cells. The underlying bone extends through the margin of **articular cartilage** into the supporting cancellous bone of the proximal or distal hemi-joint, and has dimensions and shape conforming to the SJ to be repaired. The exogenous osteogenic protein is deposited on the matrix surface to induce formation of new distinct tissues, and to permit **regeneration** of a functional SJ replacement comprising distinct tissues.

INDEPENDENT CLAIMS are also included for the following:
(1) a **method** for inducing the formation of a replacement skeletal joint which is mechanically and functional[redacted] viable by implanting the above device into a mammal;
(2) a **method** for repairing, in vivo, an **articular cartilage** defect; and
(3) a **method** for repairing, in vivo, a non-mineralized tissue defect in a skeletal joint.
ACTIVITY - Osteopathic.
MECHANISM OF ACTION - Implant.
USE - (I) is useful for inducing the formation of a functional SJ replacement by implanting (I) at a locus in a mammal, and for repairing an **articular cartilage** defect occurring in a synovial cavity in a mammal (claimed). (I) is useful for repair and **regeneration** of distinct tissues at a single defect side in a mammal and for the manufacture, in vivo, of autogenous replacement body parts comprising distinct tissues. (I) serves as a template to form a functional replacement SJ which is long term mechanically and functionally viable.
ADVANTAGE - A cartilage defect in an articulating joint, particularly a superficial **articular cartilage** defect can be functionally restored and the undesirable formation of fibrocartilage as in conventional methods, or degeneration into a full-thickness defect can be avoided. (I) induces formation of bona fide hyaline cartilage rather than fibrocartilage at a defect site.
Dwg.0/4

ACCESSION NUMBER: 2000-571418 [53] WPIX
CROSS REFERENCE: 1996-039987 [04]; 2000-222942 [19]
DOC. NO. NON-CPI: N2000-422681
DOC. NO. CPI: C2000-170290
TITLE: Device for repairing skeletal joint defect in mammals comprises exogenous osteogenic protein deposited on the surface of a matrix comprising plural distinct tissues derived from proximal or distal hemi-joint.
DERWENT CLASS: A96 B04 D22 P32
INVENTOR(S): KHOURI, R K; RUEGER, D C; SAMPATH, K T
PATENT ASSIGNEE(S): (STYC) STRYKER CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6110482	A	20000829	(200053)*		21

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6110482	A	CIP of	US 1994-253398	19940603
			US 1995-459129	19950602

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6110482	A	CIP of	US 5906827

PRIORITY APPLN. INFO: US 1995-459129 19950602; US 1994-253398 19940603

L4 ANSWER 30 OF 31 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

TI **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.

AN 2000-514778 [46] WPIX

AB WO 200044413 A UPAB: 20000921

NOVELTY - **Regeneration** of **articular cartilage** comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein (BMP).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition for **regeneration** of **articular cartilage** comprising at least one BMP.

USE - For regenerating **articular cartilage** injury or defect. The **method** can also be used for the treatment of osteoarthritis which will delay or reduce the need for artificial hip replacements.

ADVANTAGE - This new **method** provides effective repair of articulate cartilage defects and injuries without the need to collect autologous tissue from the patient. Current therapeutic strategies are based on grafting chondral and osteochondral tissues. However, donor tissue is limited and requires surgery at a second site to harvest tissue for implant. As the BMP's can be produced by recombinant DNA technology they are of unlimited supply.

Dwg.0/0

ACCESSION NUMBER: 2000-514778 [46] WPIX
DOC. NO. NON-CPI: N2000-380459
DOC. NO. CPI: C2000-153579
TITLE: **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
DERWENT CLASS: B04 P34
INVENTOR(S): MORRIS, E; PELUSO, D; ZHANG, R
PATENT ASSIGNEE(S): (GEMY) GENETICS INST INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044413	A1	20000803	(200046)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000027483	A	20000818	(200057)		
NO 2001003744	A	20010918	(200169)		
EP 1148897	A1	20011031	(200172)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000007892	A	20011030	(200173)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000044413	A1	WO 2000-US2430	20000131
AU 2000027483	A	AU 2000-27483	20000131
NO 2001003744	A	WO 2000-US2430	20000131
		NO 2001-3744	20010731

EP 1148897	A1	EP 2000-905869	20000131
		WO 2000-US2430	20000131
BR 2000007892 A		BR 2000-7892	20000131
		WO 2000-US2430	20000131

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000027483 A		Based on	WO 200044413
EP 1148897	A1	Based on	WO 200044413
BR 2000007892 A		Based on	WO 200044413

PRIORITY APPLN. INFO: US 2000-493543 20000128; US 1999-118160P 19990201

L4 ANSWER 31 OF 31 TOXLIT

TI Methods and compositions comprising bone morphogenetic proteins for healing and repair of **articular cartilage**.

AB Methods and compns. are provided for the treatment of **articular cartilage** defects and disease involving the combination of the tissue, such as osteochondral grafts, with active growth factor. The active growth factor is preferably a compn. contg. at least one **bone morphogenetic protein** and a suitable carrier. The **method** results in the **regeneration** of functional repair of **articular cartilage** tissue. Osteochondral grafts (3.5 mm diam.) were harvested from the trochlear groove of the medial femoral condyle of rabbit donors, and transplanted into a 3.5 mm deep defect in the trochlear groove of rabbit recipients. The grafts were bathed in either rhBMP-2 (0.5 mg/mL) or buffer control prior to implantation. Rabbits were sacrificed 4 wk after surgery and the transplants and surrounding tissues were evaluated by a histol.-histochem. grading scale. On growth examn., the joints showed no sign of inflammation. All the defects were filled by repair tissue, and the healing of the defects in the rhBMP-2-treated group was significantly improved as compared to that in the control group.

ACCESSION NUMBER: 2000:52093 TOXLIT
DOCUMENT NUMBER: CA-133-140314V
TITLE: Methods and compositions comprising bone morphogenetic proteins for healing and repair of **articular cartilage**.
AUTHOR: Zhang R; Peluso D; Morris E
SOURCE: (2000). PCT Int. Appl. PATENT NO. 0044413 08/03/2000 (Genetics Institute, Inc.). CODEN: PIXXD2.
PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 133:140314
ENTRY MONTH: 200008

=> d his

(FILE 'HOME' ENTERED AT 12:03:02 ON 14 JAN 2002)

FILE 'MEDLINE, USPATFULL, WPIDS, WPIX, TOXLIT, JAPIO, JICST-EPLUS, FSTA, FROSTI, BIOBUSINESS, CANCERLIT, DIOGENES, TOXCENTER, BIOSIS, BIOTECHDS, PHAR, CEN, CEABA-VTB, EMBASE, DGENE, SCISEARCH' ENTERED AT 12:05:11 ON 14 JAN 2002

L1 15310 S BONE MORPHOGENETIC PROTEIN
L2 1060 S ARTICU[redacted]R CARTILAGE AND REGENERATION
L3 71 S L2 AND L1
L4 31 S L3 AND METHOD

=> d l3 ti abs ibib 1-10

L3 ANSWER 1 OF 71 MEDLINE
TI Cartilage and bone **regeneration** using gene-enhanced tissue engineering.
AB Joint cartilage injury remains a major problem in orthopaedics with more than 500,000 cartilage repair procedures performed yearly in the United States at a cost of hundreds of millions of dollars. No consistently reliable means to regenerate joint cartilage currently exists. The technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human bone morphogenic protein-7 complementary deoxyribonucleic acid into periosteal-derived rabbit mesenchymal stem cells. Bone morphogenic protein-7 secreting gene modified cells subsequently were expanded in monolayer culture, seeded onto polyglycolic acid grafts, implanted into a rabbit knee osteochondral defect model, and evaluated for bone and cartilage repair after 4, 8, and 12 weeks. The grafts containing bone morphogenic protein-7 gene modified cells consistently showed complete or near complete bone and **articular cartilage regeneration** at 8 and 12 weeks whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria. This is the first report of **articular cartilage regeneration** using a combined gene therapy and tissue engineering approach.
ACCESSION NUMBER: 2000488818 MEDLINE
DOCUMENT NUMBER: 20492911 PubMed ID: 11039767
TITLE: Cartilage and bone **regeneration** using gene-enhanced tissue engineering.
AUTHOR: Mason J M; Breitbart A S; Barcia M; Porti D; Pergolizzi R G; Grande D A
CORPORATE SOURCE: Department of Research, North Shore University Hospital-New York University School of Medicine, Manhasset 11030, USA.
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (2000 Oct) (379 Suppl) S171-8.
Journal code: DFY. ISSN: 0009-921X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001103

L3 ANSWER 2 OF 71 MEDLINE
TI Use of recombinant human osteogenic protein-1 for the repair of subchondral defects in **articular cartilage** in goats.
AB The objective of this pilot study was to examine in vivo the potential of recombinant human osteogenic protein-1 (rhOP-1, also called **bone morphogenetic protein**-7, BMP-7) for treatment of subchondral lesions by induction of new hyaline cartilage formation. Subchondral left knee defects in 17 mature goats were treated with fresh coagulated blood mixed with (1) rhOP-1 combined with collagen (OP-1

device, 400 microgram/mL); (2) rhOP-1 alone (OP-1 peptide, 200 microgram/mL); (3) OP-1 device with small particles of autologous ear perichondrium; (4) OP-1 peptide with small particles of autologous ear perichondrium; or (5) autologous ear perichondrium alone (controls). rhOP-1 was combined with either collagen (OP-1 device) or not (OP-1 peptide). The defects were closed with a periosteal flap. The formation of cartilage tissue was studied by histologic and biochemical evaluation at 1, 2, and 4 months after implantation. One and 2 months after implantation there were no obvious differences between control and rhOP-1-treated defects. Four months after implantation, only one out of three controls (without rhOP-1) showed beginning signs of cartilage formation while all four rhOP-1-treated defects were completely or partly filled with cartilage. A significant linear relationship was found between rhOP-1 concentration and the total amount of aggrecan in the defects. These results suggest that implantation of rhOP-1 promotes cartilage formation in subchondral defects in goats at 4 months after implantation. Therefore, rhOP-1 could be a novel factor for **regeneration** of cartilage in **articular cartilage** defects.

ACCESSION NUMBER: 2000069774 MEDLINE
DOCUMENT NUMBER: 20069774 PubMed ID: 10602084

TITLE: Use of recombinant human osteogenic protein-1 for the repair of subchondral defects in **articular cartilage** in goats.

AUTHOR: Louwerse R T; Heyligers I C; Klein-Nulend J; Sugihara S; van Kampen G P; Semeins C M; Goei S W; de Koning M H; Wuisman P I; Burger E H
CORPORATE SOURCE: Department of Orthopaedic Surgery, Academic Hospital Vrije Universiteit, Amsterdam, The Netherlands.

SOURCE: JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (2000 Mar 15) 49 (4) 506-16.
Journal code: HJJ; 0112726. ISSN: 0021-9304.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000210

L3 ANSWER 3 OF 71 MEDLINE

TI **Articular cartilage regeneration** using periosteum.

AB Periosteum has chondrogenic potential that makes it possible to repair or regenerate cartilage in damaged joints. Whole periosteal explants also can be cultured in vitro for the purpose of studying chondrogenesis. This chondrogenic potential arises because the cambium layer of periosteum contains chondrocyte precursor cells that form cartilage during limb development and growth in utero, and does so once again during fracture healing. The advantages of whole tissue periosteal transplants for cartilage repair include the fact that this tissue meets the three primary requirements for tissue engineering: a source of cells, a scaffold for delivering and retaining them, and a source of local growth factors. Data from in vivo studies show that periosteum transplanted into osteochondral articular defects produce cartilage that can restore the **articular cartilage** and be replaced by bone in the subchondral region. This capacity is determined by surgical factors such as the orientation of the cambium layer, postoperative factors such as the use of continuous passive

motion, and the age and maturity of the experimental animal. In vitro studies have shown that the chondrogenic potential of periosteal explants is determined by culture, donor conditions, and technical factors. Chondrogenesis is optimized by suspension of the explants in agarose under aerobic conditions, with supplementation of the media using fetal calf serum and growth factors, particularly transforming growth factor-beta 1. The role of physical factors currently is being investigated, but studies show that the mechanical environment is important. Donor factors that are important include the harvest site, the size of the periosteal explant, and most importantly the age of the donor. Periosteal chondrogenesis follows a specific time course of events, with proliferation preceding differentiation. The current challenge is to clarify the process of periosteal chondrogenesis and its regulation at the cellular and molecular levels, so that it can be controlled intelligently and optimized for the purpose of cartilage repair and **regeneration**.

ACCESSION NUMBER: 2000013970 MEDLINE
DOCUMENT NUMBER: 20013970 PubMed ID: 10546647
TITLE: **Articular cartilage regeneration** using periosteum.
AUTHOR: O'Driscoll S W
CORPORATE SOURCE: Department of Orthopedic Surgery, Mayo Clinic, Mayo Foundation, Rochester, MN 55905, USA.
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (1999 Oct) (367 Suppl) S186-203. Ref: 108
Journal code: DFY; 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991118

L3 ANSWER 4 OF 71 MEDLINE
TI Tissue engineering principles in orthopaedic surgery.
AB Advances in the fields of biotechnology and biomaterials offer the orthopaedic surgeon the exciting possibility of repair or **regeneration** of tissue lost to injury, disease, or aging. The promising area of tissue engineering represents a multidisciplinary approach aimed at solving some of the most perplexing biologic problems, namely, the creation of new tissues and organs similar to the original tissues and organs. In addition, strategies using new synthetic polymer formulations can facilitate tissue replacement and represent alternatives to tissue **regeneration** in certain conditions. Although biotechnology has broad application over many medical specialties, orthopaedics is receiving a large focus of the research effort devoted to techniques for developing bone, **articular cartilage**, ligaments, and tendons. Because bioengineered tissue and/or techniques to stimulate tissue **regeneration** soon may be used clinically, orthopaedic surgeons should have a working knowledge of the basic concepts involved. Terms, such as biomaterial, biotechnology, matrices of synthetic or biologic polymers or both, adhesion, cohesion, porosity, induction, conduction, stem cell, progenitor cell, mesenchymal cell, tissue growth factor, **bone morphogenetic protein**, mitogenic and chemotactic factors, and numerous other terms will become part of the working language of clinicians of the twenty-first century.

ACCESSION NUMBER: 2000013957 MEDLINE
DOCUMENT NUMBER: 20[redacted]3957 PubMed ID: 10546634
TITLE: T[redacted]ue engineering principles in o[redacted]opaedic surgery.
AUTHOR: Jackson D W; Simon T M
CORPORATE SOURCE: Southern California Center for Sports Medicine, Long Beach,
USA.
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (1999 Oct) (367
Suppl) S31-45.
Journal code: DFY; 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991118

bad date

L3 ANSWER 5 OF 71 MEDLINE
TI N,N-dicarboxymethyl chitosan as delivery agent for **bone morphogenetic protein** in the repair of **articular cartilage**.
AB **Bone morphogenetic protein** (BMP), associated with N,N-dicarboxymethyl chitosan, is used to induce or facilitate the repair of **articular cartilage** lesions. This association is intended for the synergistic potentiation of the respective biological effects. Data show that BMP-7 enhances the in vivo proliferation of cells with chondrocytes phenotype in the articular environment, leading to partial healing of the articular surface of the lesions. N,N-dicarboxymethyl chitosan is found to be useful as a molecular carrier or drug delivery agent.
ACCESSION NUMBER: 1999325177 MEDLINE
DOCUMENT NUMBER: 99325177 PubMed ID: 10396855
TITLE: N,N-dicarboxymethyl chitosan as delivery agent for **bone morphogenetic protein** in the repair of **articular cartilage**.
AUTHOR: Mattioli-Belmonte M; Gigante A; Muzzarelli R A; Politano R;
De Benedittis A; Specchia N; Buffa A; Biagini G; Greco F
CORPORATE SOURCE: Institute of Normal Human Morphology, Faculty of Medicine, University of Ancona, Italy.. belmonte@popsci.unian.it
SOURCE: MEDICAL AND BIOLOGICAL ENGINEERING AND COMPUTING, (1999 Jan) 37 (1) 130-4.
Journal code: LPN; 7704869. ISSN: 0140-0118.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990730
Last Updated on STN: 19990730
Entered Medline: 19990720

L3 ANSWER 6 OF 71 MEDLINE
TI Stimulation of cartilage differentiation by osteogenic protein-1 in cultures of human perichondrium.
AB Exposure of progenitor cells with chondrogenic potential to recombinant human osteogenic protein-1 [rhOP-1, or **bone morphogenetic protein**-7 (BMP-7)] may be of therapeutic interest in the **regeneration** of **articular**

cartilage. Therefore, in this study, we examined the influence of rhOP-1 on cartila[redacted] formation by human perichondri[redacted] tissue containing progenitor cells [redacted]th chondrogenic potential in v[redacted]o. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had been added or not (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP-1. Cartilage formation was monitored biochemically by measuring [&sup35;S]sulfate incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [&sup35;S]sulfate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 microgram/ml. Histology revealed that explants treated with 20-200 microgram/ml rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. These results suggest that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct actions of rhOP-1 on perichondrium cells to stimulate chondrocytic differentiation and production of cartilage matrix in vitro provide a cellular mechanism for the induction of cartilage formation by rhOP-1 in vivo. Thus, rhOP-1 may promote early steps in the cascade of events leading to cartilage formation. Therefore, rhOP-1 could be an interesting factor for **regeneration** of cartilage in **articular cartilage** defects.

ACCESSION NUMBER: 1999055466 MEDLINE
DOCUMENT NUMBER: 99055466 PubMed ID: 9836793
TITLE: Stimulation of cartilage differentiation by osteogenic protein-1 in cultures of human perichondrium.
AUTHOR: Klein-Nulend J; Semeins C M; Mulder J W; Winters H A; Goei S W; Ooms M E; Burger E H
CORPORATE SOURCE: Department of Oral Cell Biology, ACTA-Vrije Universiteit, 1081 BT Amsterdam, The Netherlands.
SOURCE: TISSUE ENGINEERING, (1998 Fall) 4 (3) 305-13.
Journal code: C70; 9505538. ISSN: 1076-3279.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990209

L3 ANSWER 7 OF 71 MEDLINE
TI Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in vitro.
AB The objective of this study was to examine in vitro the influence of recombinant human osteogenic protein-1 [rhOP-1, or **bone morphogenetic protein**-7 (BMP-7)] on cartilage formation by human and goat perichondrium tissue containing progenitor cells with chondrogenic potential. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had been added or not added (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP-1. Cartilage formation was monitored biochemically by measuring [35S]-sulphate incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [35S]-sulphate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 microg/mL (human explants: +148%; goat explants: +116%). Histology revealed that explants treated with 20-200 microg/mL of rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. It was

concluded that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct actions of rhOP-1 on perichondrium cells in the stimulation of chondrocytic differentiation and production of cartilage matrix in vitro provides a cellular mechanism for the induction of cartilage formation by rhOP-1 in vivo. Thus rhOP-1 may promote early steps in the cascade of events leading to cartilage formation and could prove to be an interesting factor in the **regeneration** of cartilage in **articular cartilage** defects.

ACCESSION NUMBER: 1998258985 MEDLINE
DOCUMENT NUMBER: 98258985 PubMed ID: 9599038
TITLE: Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in vitro.
AUTHOR: Klein-Nulend J; Louwerse R T; Heyligers I C; Wuisman P I; Semeins C M; Goei S W; Burger E H
CORPORATE SOURCE: ACTA-Vrije Universiteit, Department of Oral Cell Biology, Amsterdam, The Netherlands..
J.Klein_Nulend.OCB.ACTA@med.vu.nl
SOURCE: JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (1998 Jun 15) 40 (4) 614-20.
Journal code: HJJ; 0112726. ISSN: 0021-9304.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980923

L3 ANSWER 8 OF 71 MEDLINE
TI **Regeneration** of **articular cartilage** defects in rabbits by osteogenic protein-1 (**bone morphogenetic protein**-7).
AB Osteogenic protein-1 (OP-1, BMP-7), a member of the transforming growth factor-beta family, induces cartilage and bone formation when implanted at intra and extraskeletal sites in vivo. The human OP-1 gene has been cloned and biologically active recombinant OP-1 homodimers have been produced. In the present study, the authors investigated the influence of OP-1 on healing of full-thickness **articular cartilage** defects, made by drilling two adjacent (phi 3mm) holes through **articular cartilage** of NZW rabbit knee joint were dissected and examined histomorphometrically. Results indicated that OP-1 induced **articular cartilage** healing and **regeneration** of the joint surface which contained cells resembling mature joint chondrocytes. These data imply a new strategy for biological repair of damaged joint surfaces in humans.
ACCESSION NUMBER: 97270218 MEDLINE
DOCUMENT NUMBER: 97270218 PubMed ID: 9115099
TITLE: **Regeneration** of **articular cartilage** defects in rabbits by osteogenic protein-1 (**bone morphogenetic protein**-7).
AUTHOR: Grgic M; Jelic M; Basic V; Basic N; Pecina M; Vukicevic S
CORPORATE SOURCE: Drago Perovic Institute of Anatomy, School of Medicine, University of Zagreb, Croatia.
SOURCE: ACTA MEDICA CROATICA, (1997) 51 (1) 23-7.
Journal code: BH2; 9208249. ISSN: 1330-0164.
PUB. COUNTRY: Croatia
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 1995
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19990129
Entered Medline: 19970514

L3 ANSWER 9 OF 71 USPATFULL
TI Methods and articles for regenerating living tissue
AB There are numerous medical situations involving deficiencies of living tissue and where increase of living tissue mass is desired. Methods are described wherein a configured, shell-like device that is capable of being penetrated by living cells and tissues, is implanted into the body of a mammal in such a way as to establish a space, the space being at least partly, bounded by the device. The configuration of the device is such that the configuration of the established space is essentially the same as the configuration of living tissue that is desired for treatment of the tissue deficiency. At least one tissue stimulating molecular substance is placed within the established space for the purpose of stimulating the growth of desired living tissue within the established space. A kit for the generation of desired living tissue, comprised of the components mentioned above, is also disclosed.

ACCESSION NUMBER: 2001:226051 USPATFULL
TITLE: Methods and articles for regenerating living tissue
INVENTOR(S): Hardwick, William R., Flagstaff, AZ, United States
Thomson, Robert C., Flagstaff, AZ, United States
Cleek, Robert L., Flagstaff, AZ, United States
Mane, Shrikant M., Flagstaff, AZ, United States
Cook, Alonzo D., Flagstaff, AZ, United States
PATENT ASSIGNEE(S): Gore Enterprise Holdings, Inc., Newark, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6328765	B1	20011211	
APPLICATION INFO.:	US 1998-205521		19981203	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Willse, David H.
ASSISTANT EXAMINER: Stewart, Alvin
LEGAL REPRESENTATIVE: Sheets, Eric J
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 25 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2632

L3 ANSWER 10 OF 71 USPATFULL
TI Pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof
AB The invention is in the area of pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof. In particular, the invention includes isolated adipose tissue derived stromal cells that have been induced to express at least one phenotypic characteristic of a neuronal, astroglial, hematopoietic progenitor, or hepatic cell. The invention also includes an isolated adipocyte tissue-derived stromal cell that has been dedifferentiated such that there is an absence of adipocyte phenotypic markers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2001:188204 USPATFULL
TITLE: Pleuripotent stem cells generated from adipose tissue-derived stromal cells and uses thereof
INVENTOR(S): Wilkison, William O., Bahama, NC, United States
Gimble, Jeffrey, Chapel Hill, NC, United States

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001033834	A1	20011025
APPLICATION INFO.:	US 2001-793173	A1	20010226 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-185338	20000226 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Sherry M. Knowles, Esq., KING & SPALDING, 45th Floor, 191 Peachtree Street, N.E., Atlanta, GA, 30303
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
LINE COUNT: 1236
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 12:03:02 ON 14 JAN 2002)

FILE 'MEDLINE, USPATFULL, WPIDS, WPIX, TOXLIT, JAPIO, JICST-EPLUS, FSTA, FROSTI, BIOBUSINESS, CANCERLIT, DIOGENES, TOXCENTER, BIOSIS, BIOTECHDS, PHAR, CEN, CEABA-VTB, EMBASE, DGENE, SCISEARCH' ENTERED AT 12:05:11 ON 14
JAN 2002
L1 15310 S BONE MORPHOGENETIC PROTEIN
L2 1060 S ARTICULAR CARTILAGE AND REGENERATION
L3 71 S L2 AND L1
L4 31 S L3 AND METHOD

=> d l3 ti abs ibib 60-71

L3 ANSWER 60 OF 71 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI Development and **regeneration** of the musculoskeletal system.
AB Skeletal development requires precise coordination of embryonic programs that regulate cell proliferation, cell differentiation, extracellular matrix remodeling, apoptosis, and angiogenesis. Growing evidence indicates that many of the genetic pathways controlling skeletal formation are also induced postnatally in response to injury. The clinical significance of this observation is clear: by understanding the molecular and cellular basis of fetal skeletogenesis, we can effectively develop therapeutic strategies for the treatment of musculoskeletal injuries, defects, and diseases in adults. This review discusses the results from several recent gene targeting experiments in mice, including Cbfal, GelB, Ihh, and Noggin, which have expanded our understanding of cartilage and bone formation, as well as soft and hard tissue repair. These analyses reveal that different components of the skeleton are generated via independent developmental pathways and unique programs of molecular regulation. Unraveling the connections among these processes will undoubtedly facilitate our ability to regenerate cartilage and bone.
ACCESSION NUMBER: 1999038136 EMBASE
TITLE: Development and **regeneration** of the musculoskeletal system.

AUTHOR: Schneider R.A.; Helms J.A.
CORPORATE SOURCE: Dr. R.A. Schneider, Department of Growth and Development, School of Dentistry, University of California, San Francisco, CA, United States
SOURCE: Current Opinion in Orthopaedics, (1998) 9/6 (20-24).
Refs: 37
ISSN: 1041-9918 CODEN: COORE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 61 OF 71 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI The healing and **regeneration** of **articular cartilage**.
ACCESSION NUMBER: 1999010803 EMBASE
TITLE: The healing and **regeneration** of **articular cartilage**.
AUTHOR: O'Driscoll S.W.
CORPORATE SOURCE: Dr. S.W. O'Driscoll, Cartilage/Connect. Tissue Res. Lab., Department of Orthopedic Surgery, Mayo Clinic, 200 First Street S.W., Rochester, MN 55905, United States. odriscoll.shawn@mayo.edu
SOURCE: Journal of Bone and Joint Surgery - Series A, (1998) 80/12 (1795-1812).
Refs: 255
ISSN: 0021-9355 CODEN: JBJSA3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English

L3 ANSWER 62 OF 71 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI Cartilage-derived morphogenetic proteins and cartilage morphogenesis.
AB Cartilage morphogenesis is a prerequisite for skeletal development and maintenance. The morphogenesis of cartilage determines the shape of bones, and joints including **articular cartilage**, ligaments, and tendon. This article reviews the recent advances in cartilage-derived morphogenetic proteins (CDMPs) and related bone morphogenetic proteins (BMPs). Cartilage-derived morphogenetic proteins (CDMPs) are related to BMPs and are critical for cartilage and joint morphogenesis. Cartilage morphogenesis is a multistep cascade that includes factors for initiation, promotion, and maintenance of cartilage phenotype. The extracellular matrix of cartilage consists of a constellation of macromolecules as collagens, proteoglycans, and glycoproteins. Morphogens bind to extracellular matrix components and assemble a morphogenetic scaffold. Recent advances in CDMPs may aid in **articular cartilage** repair and **regeneration**.
ACCESSION NUMBER: 1998385022 EMBASE
TITLE: Cartilage-derived morphogenetic proteins and cartilage morphogenesis.
AUTHOR: Reddi A.H.
CORPORATE SOURCE: A.H. Reddi, Res. Bldg. 1, 4635 Second Avenue, Sacramento, CA 95817, United States. ahreddi@uscaavis.edu
SOURCE: Microscopy Research and Technique, (15 Oct 1998) 43/2 (131-136).
Refs: 73
ISSN: 1059-910X CODEN: MRTEEO
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
[redacted] Developmental Biology and Teratology
[redacted] Clinical Biochemistry
033 Orthopedic Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 63 OF 71 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI Stimulation of cartilage differentiation by osteogenic protein-1 in cultures of human perichondrium.
AB Exposure of progenitor cells with chondrogenic potential to recombinant human osteogenic protein-1 [rhOP-1, or **bone morphogenetic protein**-7 (BMP-7] may be of therapeutic interest in the **regeneration** of **articular cartilage**. Therefore, in this study, we examined the influence of rhOP-1 on cartilage formation by human perichondrium tissue containing progenitor cells with chondrogenic potential in vitro. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had been added or not (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP1. Cartilage formation was monitored biochemically by measuring [35S]sulfate incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [35S]sulfate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 .mu.g/ml. Histology revealed that explants treated with 20-200 .mu.g/ml rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. These results suggest that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct actions of rhOP-1 on perichondrium cells to stimulate chondrocytic differentiation and production of cartilage matrix in vitro provide a cellular mechanism for the induction of cartilage formation by rhOP-1 in vivo. Thus, rhOP-1 may promote early steps in the cascade of events leading to cartilage formation. Therefore, rhOP-1 could be an interesting factor for **regeneration** of cartilage in **articular cartilage** defects.
ACCESSION NUMBER: 1998342634 EMBASE
TITLE: Stimulation of cartilage differentiation by osteogenic protein-1 in cultures of human perichondrium.
AUTHOR: Klein-Nulend J.; Semeins C.M.; Mulder J.W.; Winters H.A.H.;
Goei S.W.; Ooms M.E.; Burger E.H.
CORPORATE SOURCE: Dr. J. Klein-Nulend, ACTA-Vrije Universiteit, Department of
Oral Cell Biology, Van der Boechorststraat 7, 1081 BT Amsterdam, Netherlands
SOURCE: Tissue Engineering, (1998) 4/3 (305-313).
Refs: 17
ISSN: 1076-3279 CODEN: TIENFP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 64 OF 71 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in vitro.
AB The objective of this study was to examine in vitro the influence of recombinant human osteogenic protein-1 [rhOP-1, or **bone**

morphogenetic protein-7 (BMP-7)] on cartilage formation by human and goat perichondrium tissue containing progenitor cells with chondrogenic potential. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had been added or not added (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP-1. Cartilage formation was monitored biochemically by measuring [35S]-sulphate incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [35S]-sulphate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 .mu.g/mL (human explants: +148%; goat explants: +116%). Histology revealed that explants treated with 20-200 .mu.g/mL of rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. It was concluded that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct actions of rhOP-1 on perichondrium cells in the stimulation of chondrocytic differentiation and production of cartilage matrix in vitro provides a cellular mechanism for the induction of cartilage formation by rhOP-1 in vivo. Thus rhOP-1 may promote early steps in the cascade of events leading to cartilage formation and could prove to be an interesting factor in the **regeneration** of cartilage in **articular cartilage** defects.

ACCESSION NUMBER: 1998165243 EMBASE
TITLE: Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in vitro.
AUTHOR: Klein-Nulend J.; Louwerse R.T.; Heyligers I.C.; Wuisman P.I.J.M.; Semeins C.M.; Goei S.W.; Burger E.H.
CORPORATE SOURCE: J. Klein-Nulend, ACTA-Vrije Universiteit, Department of Oral Cell Biology, Van der Boechorststraat 7, 1081 BT Amsterdam, Netherlands
SOURCE: Journal of Biomedical Materials Research, (15 Jun 1998) 40/4 (614-620).
Refs: 17
ISSN: 0021-9304 CODEN: JBMRBG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
021 Developmental Biology and Teratology
027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 65 OF 71 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI Biological resurfacing: An alternative to total joint arthroplasty.
AB These preliminary observations suggest that the functional repair of adult hyaline cartilage is controlled by the entrance and lineage progression of uncommitted MSCs into chondrocytes under the direction of specific biological and mechanical cues which represent a recapitulation of embryonic events. This concept implies that to some extent the **regeneration** of destroyed **articular cartilage** is limited by an inadequate supply of MSCs from the host and their inefficient interaction with the appropriate factors at the local site. Finally, the use of autologous cell tissue engineering could provide the basis of an important application for the repair of deficient joint surfaces as a result of trauma or osteoarthritis.

ACCESSION NUMBER: 94290874 EMBASE
DOCUMENT NUMBER: 19[redacted]290874
TITLE: Bi[redacted]ogical resurfacing: An alternat[redacted]e to total joint arthroplasty.
AUTHOR: Goldberg V.M.; Caplan A.I.
CORPORATE SOURCE: Dept of Orthopedics, Case Western Reserve University, 2074 Abington Rd,Cleveland, OH 44106, United States
SOURCE: Orthopedics, (1994) 17/9 (819-821).
ISSN: 0147-7447 CODEN: ORTHDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 009 Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 66 OF 71 SCISEARCH COPYRIGHT 2002 ISI (R)
TI **Regeneration** of **articular cartilage** chondral defects by osteogenic protein-1 (**bone morphogenetic protein**-7) in sheep
AB The efficacy of osteogenic protein-1 (OP-1; BMP-7) in **regeneration** of **articular cartilage** was examined by creating knee chondral defects in sheep. With a specially designed instrument in both knees, two 10 mm (diameter) chondral defects were created: one in the trochlea and the other on the femoral condyle. The recombinant BMP was delivered via an extra-articulary positioned mini-osmotic pump, which was fixed to the femoral diaphysis above the knee joint, and connected by a polyethylene tubing to the articular space. Prior to use, the compatibility of OP-1 with mini-osmotic pumps was tested in vitro by measuring aggregation/precipitation and modification of the released protein by size exclusion and reversed phase RPLC. The average amount of aggregation was 15% and about 5% of OP-1 was modified. However, the biological activity of OP-1 released from pumps over a period of 2 weeks at 37 degreesC was equal to ROS cell assay OP-1 standard. Following surgery, a total of 55 mug (low dose) or 170 mug (high dose) OP-1 in acetate buffer (pH 4.5) was slowly released from the pump over a period of 2 weeks. The pumps connected to control knees were filled with acetate buffer as a vehicle. Twelve animals were operated, six of which were treated with the low OP-1 dose, and six with the high OP-1 dose. Three sheep of each group were killed either at 3 or 6 months following surgery, based on arthroscopical evaluation. The chondral defects in the control knees remained empty during the observation period. At 3 months following surgery, defects treated with both OP-1 doses were filled with connective tissue and cartilage. At 6 months following surgery, both doses of OP-1 stimulated **regeneration** in treated knees. The boundaries between new and old cartilage were well fused and mechanically resisted animals' weight bearing. The regenerated cartilage was rich in proteoglycans and type II collagen, as demonstrated by toluidine blue staining and immunohistochemistry. No signs of endochondral bone formation above the bony tidemark were observed. We suggest that a recombinant **bone morphogenetic protein** stimulates ingrowth of mesenchymal cells into the chondral defects which then transform into newly formed **articular cartilage**-like tissue.
ACCESSION NUMBER: 2002:7154 SCISEARCH
THE GENUINE ARTICLE: 502KX
TITLE: **Regeneration** of **articular cartilage** chondral defects by osteogenic protein-1

(**bone morphogenetic protein**
-[redacted]in sheep
AUTHOR: Je[redacted]c M; Pecina M; Haspl M; Kos J; [redacted]ylor K; Maticic D; McCartney J; Yin S; Rueger D; Vukicevic S (Reprint)
CORPORATE SOURCE: Univ Zagreb, Sch Med, Dept Anat, Salata 11, POB 916, Zagreb 10000, Croatia (Reprint); Univ Zagreb, Sch Med, Dept Anat, Zagreb 10000, Croatia; Univ Zagreb, Sch Med, Dept Orthopaed Surg, Zagreb 10000, Croatia; Univ Zagreb, Fac Vet, Surg Clin, Zagreb 10000, Croatia; Univ Zagreb, Fac Vet, Clin Orthopaed Surg, Zagreb 10000, Croatia; Univ Zagreb, Fac Vet, Clin Ophthalmol, Zagreb 10000, Croatia; Stryker Biotech, Hopkinton, MA 01748 USA; Creat Biomol, Hopkinton, MA 01748 USA
COUNTRY OF AUTHOR: Croatia; USA
SOURCE: GROWTH FACTORS, (DEC 2001) Vol. 19, No. 2, pp. 101-113. Publisher: HARWOOD ACAD PUBL GMBH, TAYLOR & FRANCIS GROUP,
325 CHESTNUT ST, 8TH FL, PHILADELPHIA, PA 19106 USA.
ISSN: 0897-7194.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 41
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L3 ANSWER 67 OF 71 SCISEARCH COPYRIGHT 2002 ISI (R)
TI FT-IR imaging spectroscopy of genetically modified bovine chondrocytes
AB Repair of **articular cartilage** defects remains a challenging problem in orthopaedic surgery. Although novel tissue engineering technologies have facilitated the synthesis of cartilage-like tissue for implantation into defect sites, questions persist as to how to best evaluate the integration of these matrices into cartilage and to assess their capability for **regeneration** and repair of the tissue. In the current study, Fourier transform infrared imaging spectroscopy (FT-IRI) was utilized to study compositional changes in genetically modified bovine chondrocytes. With this technique, it was possible to evaluate the integration of the newly formed matrix into the **articular cartilage** substrate, and the content and distribution of the collagen and proteoglycan components in the repair tissue compared to native **articular cartilage**. Bovine chondrocytes were treated with an adenovirus (Ad) vector encoding **bone morphogenetic protein**-7 (AdBMP-7), transplanted onto bovine cartilage explants in vitro and the matrix evaluated by FT-IRI after 3 weeks of growth. Data were acquired from a 400 X 400-mum region of a histological specimen at 7-mum spatial resolution. FT-IR images were created based on collagen and proteoglycan content. It was apparent from these images that the AdBMP-7-treated chondrocyte matrix produced significantly more proteoglycan compared to both naive chondrocyte matrix, and to native bovine **articular cartilage**. However, the distribution of proteoglycan was very heterogeneous. In contrast, there was significantly less type II collagen in both AdBMP-7 and in naive chondrocyte matrix compared to the **articular cartilage** substrate. Overall, the new information obtained by FT-IR imaging spectroscopy will facilitate in design of new materials for cartilage **regeneration** and repair.

ACCESSION NUMBER: 2001:887358 SCISEARCH
THE GENUINE ARTICLE: 487RD
TITLE: FT-IR imaging spectroscopy of genetically modified bovine chondrocytes
AUTHOR: Camacho N P; West P; Griffith M H; Warren R F; Hidaka C (Reprint)
CORPORATE SOURCE: Hosp Special Surg, Lab Soft Tissue Res, Div Res, 535 E

70th St, New York, NY 10021 USA (Reprint); Hosp Special S[redacted], Lab Soft Tissue Res, Div Res, New York, NY 10021 USA
COUNTRY OF AUTHOR: USA
SOURCE: MATERIALS SCIENCE & ENGINEERING C-BIOMIMETIC AND SUPRAMOLECULAR SYSTEMS, (1 NOV 2001) Vol. 17, No. 1-2, Sp. iss. SI, pp. 3-9.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0928-4931.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 23
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L3 ANSWER 68 OF 71 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Use of recombinant human osteogenic protein-1 for the repair of subchondral defects in **articular cartilage** in goats
AB The objective of this pilot study was to examine in vivo the potential of recombinant human osteogenic protein-1 (rhOP-1, also called **bone morphogenetic protein**-7, BMP-7) for treatment of subchondral lesions by induction of new hyaline cartilage formation. Subchondral left knee defects in 17 mature goats were treated with fresh coagulated blood mixed with (1) rhOP-1 combined with collagen (OP-1 device, 400 mu g/mL); (2) rhOP-1 alone (OP-1 peptide, 200 mu g/mL); (3) OP-1 device with small particles of autologous ear perichondrium; (4) OP-1 peptide with small particles of autologous ear perichondrium; or (5) autologous ear perichondrium alone (controls). rhOP-1 was combined with either collagen (OP-1 device) or not (OP-1 peptide). The defects were closed with a periosteal flay. The formation of cartilage tissue was studied by histologic and biochemical evaluation at 1, 2, and 4 months after implantation. One and 2 months after implantation there were no obvious differences between control and rhOP-1-treated defects. Four months after implantation, only one out of three controls (without rhOP-1) showed beginning signs of cartilage formation while all four rhOP-1-treated defects were completely or partly filled with cartilage. A significant linear relationship was found between rhOP-1 concentration and the total amount of aggrecan in the defects. These results suggest that implantation of rhOP-1 promotes cartilage formation in subchondral defects in goats at 4 months after implantation. Therefore, rhOP-1 could be a novel factor for **regeneration** of cartilage in **articular cartilage** defects. (C) 2000 John Wiley & Sons, Inc.
ACCESSION NUMBER: 2000:27372 SCISEARCH
THE GENUINE ARTICLE: 270AE
TITLE: Use of recombinant human osteogenic protein-1 for the repair of subchondral defects in **articular cartilage** in goats
AUTHOR: Louwerse R T; Heyligers I C; KleinNulend J; Sugihara S; vanKampen G P J; Semeins C M; Goei S W; deKoning M H M T; Wuisman P I J M; Burger E H (Reprint)
CORPORATE SOURCE: ACTA VRIJE UNIV AMSTERDAM, DEPT ORAL CELL BIOL, VAN DER BOECHORSTSTR 7, NL-1081 BT AMSTERDAM, NETHERLANDS (Reprint); ACTA VRIJE UNIV AMSTERDAM, DEPT ORAL CELL BIOL, NL-1081 BT AMSTERDAM, NETHERLANDS; JAN VAN BREEMEN INST, CTR RHEUMATOL & REHABIL, AMSTERDAM, NETHERLANDS; VRIJE UNIV AMSTERDAM, ACAD HOSP, DEPT ORTHOPAED SURG, AMSTERDAM, NETHERLANDS
COUNTRY OF AUTHOR: NETHERLANDS

SOURCE: JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (15 MAR 1999) V[redacted] 49, No. 4, pp. 506-516.
P[redacted]lisher: JOHN WILEY & SONS INC, THIRD AVE, NEW YORK,
NY 10158-0012.
ISSN: 0021-9304.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 34
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L3 ANSWER 69 OF 71 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Tissue engineering principles in orthopaedic surgery
AB Advances in the fields of biotechnology and biomaterials offer the orthopaedic surgeon the exciting possibility of repair or **regeneration** of tissue lost to injury, disease, or aging. The promising area of tissue engineering represents a multidisciplinary approach aimed at solving some of the most perplexing biologic problems, namely, the creation of new tissues and organs similar to the original tissues and organs. In addition, strategies using new synthetic polymer formulations can facilitate tissue replacement and represent alternatives to tissue **regeneration** in certain conditions. Although biotechnology has broad application over many medical specialties, orthopaedics is receiving a large focus of the research effort devoted to techniques for developing bone, **articular cartilage**, ligaments, and tendons. Because bioengineered tissue and/or techniques to stimulate tissue **regeneration** soon may be used clinically, orthopaedic surgeons should have a working knowledge of the basic concepts involved. Terms, such as biomaterial, biotechnology, matrices of synthetic or biologic polymers or both, adhesion, cohesion, porosity, induction, conduction, stem cell, progenitor cell, mesenchymal cell, tissue growth factor, **bone morphogenetic protein**, mitogenic and chemotactic factors, and numerous other terms will become part of the working language of clinicians of the twenty-first century.
ACCESSION NUMBER: 1999:815455 SCISEARCH
THE GENUINE ARTICLE: 247RR
TITLE: Tissue engineering principles in orthopaedic surgery
AUTHOR: Jackson D W (Reprint); Simon T M
CORPORATE SOURCE: 2760 ATLANTIC AVE, LONG BEACH, CA 90806 (Reprint); SO CALIF CTR SPORTS MED, LONG BEACH, CA
COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (OCT 1999) No.
367, Supp. [S], pp. S31-S45.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0009-921X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L3 ANSWER 70 OF 71 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Stimulation of cartilage differentiation by osteogenic protein-1 in cultures of human perichondrium
AB Exposure of progenitor cells with chondrogenic potential to recombinant human osteogenic protein-1 [rhOP-1, or **bone morphogenetic protein**-7 (BMP-7] may be of therapeutic interest in the **regeneration** of **articular**

cartilage. Therefore, in this study, we examined the influence of rhOP-1 on cartila[redacted] formation by human perichondriu[redacted] tissue containing progenitor cells [redacted]th chondrogenic potential in vi[redacted]. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had been added or not (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP-1. Cartilage formation was monitored biochemically by measuring [S-35]sulfate , incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [35S]sulfate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 mu g/ml. Histology revealed that explants treated with 20-200 mu g/ml rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. These results suggest that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct actions of rhOP-1 on perichondrium cells to stimulate chondrocytic differentiation and production of cartilage matrix in vitro provide a cellular mechanism for the induction of cartilage formation by rhOP-1 in vivo. Thus, rhOP-1 may promote early steps in the cascade of events leading to cartilage formation. Therefore, rhOP-1 could be an interesting factor for **regeneration** of cartilage in **articular cartilage** defects.

ACCESSION NUMBER: 1998:792034 SCISEARCH
THE GENUINE ARTICLE: 126ZC
TITLE: Stimulation of cartilage differentiation by osteogenic protein-1 in cultures of human perichondrium
AUTHOR: KleinNulend J (Reprint); Semeins C M; Mulder J W; Winters H A H; Goei S W; Ooms M E; Burger E H
CORPORATE SOURCE: FREE UNIV AMSTERDAM, DEPT ORAL CELL BIOL, ACTA, NL-1081 BT
AMSTERDAM, NETHERLANDS; FREE UNIV AMSTERDAM, ACAD HOSP, DEPT PLAST & RECONSTRUCT SURG, NL-1081 HV AMSTERDAM, NETHERLANDS; INST RES EXTRAMURAL MED EMGO INST, NL-1081 BT
AMSTERDAM, NETHERLANDS
COUNTRY OF AUTHOR: NETHERLANDS
SOURCE: TISSUE ENGINEERING, (FAL 1998) Vol. 4, No. 3, pp. 305-313.
Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538.
ISSN: 1076-3279.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 17
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L3 ANSWER 71 OF 71 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in vitro
AB The objective of this study was to examine in vitro the influence of recombinant human osteogenic protein-1 [rhOP-1, or **bone morphogenetic protein**-7 (BMP-7)] on cartilage formation by human and goat perichondrium tissue containing progenitor cells with chondrogenic potential. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had been added or not added (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP-1. Cartilage formation was monitored biochemically by measuring [S-35]-sulphate incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [S-35]- sulphate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 mu g/mL, (human

explants: +148%; goat explants: +116%). Histology revealed that explants treated with 20-20 mu g/mL of rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. It was concluded that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct actions of rhOP-1 on perichondrium cells in the stimulation of chondrocytic differentiation and production of cartilage matrix in vitro provides a cellular mechanism for the induction of cartilage formation by rhOP-1 in vitro. Thus rhOP-1 may promote early steps in the cascade of events leading to cartilage formation and could prove to be an interesting factor in the **regeneration** of cartilage in **articular cartilage** defects. (C) 1998 John Wiley & Sons, Inc.

ACCESSION NUMBER: 1998:360067 SCISEARCH
THE GENUINE ARTICLE: ZL733
TITLE: Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in vitro
AUTHOR: KleinNulend J (Reprint); Louwerse R T; Heyligers I C; Wuisman P I J M; Semeins C M; Goei S W; Burger E H
CORPORATE SOURCE: FREE UNIV AMSTERDAM, ACTA, DEPT ORAL CELL BIOL, VAN DER BOECHORSTSTR 7, NL-1081 BT AMSTERDAM, NETHERLANDS (Reprint); FREE UNIV AMSTERDAM, ACAD HOSP, DEPT ORTHOPAED, NL-1081 BT AMSTERDAM, NETHERLANDS
COUNTRY OF AUTHOR: NETHERLANDS
SOURCE: JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (15 JUN 1998) Vol. 40, No. 4, pp. 614-620. Publisher: JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012. ISSN: 0021-9304.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 17
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> d his

(FILE 'HOME' ENTERED AT 12:03:02 ON 14 JAN 2002)

FILE 'MEDLINE, USPATFULL, WPIDS, WPIX, TOXLIT, JAPIO, JICST-EPLUS, FSTA, FROSTI, BIOBUSINESS, CANCERLIT, DIOGENES, TOXCENTER, BIOSIS, BIOTECHDS, PHAR, CEN, CEABA-VTB, EMBASE, DGENE, SCISEARCH' ENTERED AT 12:05:11 ON 14 JAN 2002

L1 15310 S BONE MORPHOGENETIC PROTEIN
L2 1060 S ARTICULAR CARTILAGE AND REGENERATION
L3 71 S L2 AND L1
L4 31 S L3 AND METHOD

=> s Vgr-2

3 FILES SEARCHED...
15 FILES SEARCHED...
L5 36 VGR-2

=> s growth differentiation factor

```
  19 FILES SEARCHED...
L6         1675 GROWTH DIFFERENTIATION FACTOR

=> s bone formation inducing protein

  15 FILES SEARCHED...
L7           18 BONE FORMATION INDUCING PROTEIN

=> s l2 and l5

L8            6 L2 AND L5

=> s l2 and l6

L9            6 L2 AND L6

=> s l2 and l7

L10           0 L2 AND L7

=> s l8 and l9

L11           0 L8 AND L9

=> d l8 ti abs ibib


L8   ANSWER 1 OF 6  USPATFULL
TI     Methods and articles for regenerating living tissue
AB     There are numerous medical situations involving deficiencies of living
       tissue and where increase of living tissue mass is desired. Methods are
       described wherein a configured, shell-like device that is capable of
       being penetrated by living cells and tissues, is implanted into the
body
       of a mammal in such a way as to establish a space, the space being at
       least partly, bounded by the device. The configuration of the device is
       such that the configuration of the established space is essentially the
       same as the configuration of living tissue that is desired for
treatment
       of the tissue deficiency. At least one tissue stimulating molecular
       substance is placed within the established space for the purpose of
       stimulating the growth of desired living tissue within the established
       space. A kit for the generation of desired living tissue, comprised of
       the components mentioned above, is also disclosed.

ACCESSION NUMBER:        2001:226051  USPATFULL
TITLE:                   Methods and articles for regenerating living tissue
INVENTOR(S):             Hardwick, William R., Flagstaff, AZ, United States
                         Thomson, Robert C., Flagstaff, AZ, United States
                         Cleek, Robert L., Flagstaff, AZ, United States
                         Mane, Shrikant M., Flagstaff, AZ, United States
                         Cook, Alonzo D., Flagstaff, AZ, United States
PATENT ASSIGNEE(S):      Gore Enterprise Holdings, Inc., Newark, Germany,
                         Federal Republic of (non-U.S. corporation)

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 6328765          B1   20011211
APPLICATION INFO.:       US 1998-205521           19981203  (9)
DOCUMENT TYPE:           Utility
FILE SEGMENT:            GRANTED
PRIMARY EXAMINER:        Willse, David H.
ASSISTANT EXAMINER:      Stewart, Alvin
LEGAL REPRESENTATIVE:    Sheets, Eric J
```

NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2632

=> d his

(FILE 'HOME' ENTERED AT 12:03:02 ON 14 JAN 2002)

FILE 'MEDLINE, USPATFULL, WPIDS, WPIX, TOXLIT, JAPIO, JICST-EPLUS, FSTA, FROSTI, BIOBUSINESS, CANCERLIT, DIOGENES, TOXCENTER, BIOSIS, BIOTECHDS, PHAR, CEN, CEABA-VTB, EMBASE, DGENE, SCISEARCH' ENTERED AT 12:05:11 ON 14
JAN 2002
L1 15310 S BONE MORPHOGENETIC PROTEIN
L2 1060 S ARTICULAR CARTILAGE AND REGENERATION
L3 71 S L2 AND L1
L4 31 S L3 AND METHOD
L5 36 S VGR-2
L6 1675 S GROWTH DIFFERENTIATION FACTOR
L7 18 S BONE FORMATION INDUCING PROTEIN
L8 6 S L2 AND L5
L9 6 S L2 AND L6
L10 0 S L2 AND L7
L11 0 S L8 AND L9

=> d l8 ti abs ibib tot

L8 ANSWER 1 OF 6 USPATFULL
TI Methods and articles for regenerating living tissue
AB There are numerous medical situations involving deficiencies of living tissue and where increase of living tissue mass is desired. Methods are described wherein a configured, shell-like device that is capable of being penetrated by living cells and tissues, is implanted into the body of a mammal in such a way as to establish a space, the space being at least partly, bounded by the device. The configuration of the device is such that the configuration of the established space is essentially the same as the configuration of living tissue that is desired for treatment of the tissue deficiency. At least one tissue stimulating molecular substance is placed within the established space for the purpose of stimulating the growth of desired living tissue within the established space. A kit for the generation of desired living tissue, comprised of the components mentioned above, is also disclosed.

ACCESSION NUMBER: 2001:226051 USPATFULL
TITLE: Methods and articles for regenerating living tissue
INVENTOR(S): Hardwick, William R., Flagstaff, AZ, United States
Thomson, Robert C., Flagstaff, AZ, United States
Cleek, Robert L., Flagstaff, AZ, United States
Mane, Shrikant M., Flagstaff, AZ, United States
Cook, Alonzo D., Flagstaff, AZ, United States
PATENT ASSIGNEE(S): Gore Enterprise Holdings, Inc., Newark, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6328765	B1	20011211	
APPLICATION INFO.:	US 1998-205521		19981203	(9)

DOCUMENT TYPE: Utility

FILE SEGMENT: GRANTED
PRIMARY EXAMINER: [redacted]llse, David H.
ASSISTANT EXAMINER: [redacted]ewart, Alvin
LEGAL REPRESENTATIVE: Sheets, Eric J
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 25 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 2632

L8 ANSWER 2 OF 6 USPATFULL
TI Bone morphogenetic protein (BMP)-9 compositions and their uses
AB Purified Bone Morphogenetic Protein (BMP)-9 proteins and processes for producing them are disclosed. The proteins may be used in the treatment of bone and cartilage defects and in wound healing and related tissue repair, and in hepatic growth and function.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2000:27958 USPATFULL
TITLE: Bone morphogenetic protein (BMP)-9 compositions and their uses
INVENTOR(S): Thies, R. Scott, Andover, MA, United States
Song, Jeffrey J., Brighton, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6034062		20000307	
APPLICATION INFO.:	US 1997-815652		19970313	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kemmerer, Elizabeth
ASSISTANT EXAMINER: Romeo, David S.
LEGAL REPRESENTATIVE: Mienert, M. C., Kapinos, Ellen J.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 2197
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 3 OF 6 USPATFULL
TI Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide and methods of inducing cartilage by
administration of same
AB Compositions of proteins with chondrocyte and cartilaginous tissue inducing activity, as well as method of using those compositions, are disclosed. The compositions comprise one or more proteins of the transforming growth factor-.beta. (TGF-.beta.) superfamily of proteins, particularly bone morphogenetic proteins (BMPs), in combination with parathyroid hormone related polypeptide (PTHrP) or an equivalent PTH-like polypeptide. The compositions and methods are useful in the treatment of osteoarthritis, cartilage defects and in related tissue repair.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 1998:154240 USPATFULL
TITLE: Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide and methods of inducing cartilage by administration of same
INVENTOR(S): Hattersley, Gary, 10 Rogers St., #303, Cambridge, MA, United States 02142
Rosen, Vicki A., 2 Cedar Rd., Chestnut Hill, MA, United

States 02167

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5846931		19981208
APPLICATION INFO.:	US 1997-926942		19970910 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-622101, filed on 26 Mar 1996, now patented, Pat. No. US 5700774
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kemmerer, Elizabeth
LEGAL REPRESENTATIVE: Lazar, Steven R.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 637
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 4 OF 6 USPATFULL
TI Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide, and methods of inducing cartilage by administration of same
AB Compositions of proteins with chondrocyte and cartilaginous tissue inducing activity, as well as method of using those compositions, are disclosed. The compositions comprise one or more proteins of the transforming growth factor-.beta. (TGF-.beta.) superfamily of proteins, particularly bone morphogenetic proteins (BMPs), in combination with parathyroid hormone related polypeptide (PTHrP) or an equivalent PTH-like polypeptide. The compositions and methods are useful in the treatment of osteoarthritis, cartilage defects and in related tissue repair.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 97:120591 USPATFULL
TITLE: Compositions comprising bone morphogenic proteins and truncated parathyroid hormone related peptide, and methods of inducing cartilage by administration of same
INVENTOR(S): Hattersley, Gary, Cambridge, MA, United States
Rosen, Vicki A., Chestnut Hill, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5700774		19971223
APPLICATION INFO.:	US 1996-622101		19960326 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Fitzgerald, David L.
ASSISTANT EXAMINER: Kemmerer, Elizabeth C.
LEGAL REPRESENTATIVE: Meinert, M. C., Lazar, S.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 668
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 5 OF 6 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
AN 2000-514778 [46] WPIDS
AB WO 200044413 A UPAB: 20000921
NOVELTY - **Regeneration** of **articular cartilage**

comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein (BMP).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is so included for a composition for **regeneration** of **articular cartilage** comprising at least one BMP.

USE - For regenerating **articular cartilage** injury or defect. The method can also be used for the treatment of osteoarthritis which will delay or reduce the need for artificial hip replacements.

ADVANTAGE - This new method provides effective repair of articulate cartilage defects and injuries without the need to collect autologous tissue from the patient. Current therapeutic strategies are based on grafting chondral and osteochondral tissues. However, donor tissue is limited and requires surgery at a second site to harvest tissue for implant. As the BMP's can be produced by recombinant DNA technology they are of unlimited supply.

Dwg.0/0

ACCESSION NUMBER: 2000-514778 [46] WPIDS
DOC. NO. NON-CPI: N2000-380459
DOC. NO. CPI: C2000-153579
TITLE: **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
DERWENT CLASS: B04 P34
INVENTOR(S): MORRIS, E; PELUSO, D; ZHANG, R
PATENT ASSIGNEE(S): (GEMY) GENETICS INST INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044413	A1	20000803	(200046)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000027483	A	20000818	(200057)		
NO 2001003744	A	20010918	(200169)		
EP 1148897	A1	20011031	(200172)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000007892	A	20011030	(200173)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000044413	A1	WO 2000-US2430	20000131
AU 2000027483	A	AU 2000-27483	20000131
NO 2001003744	A	WO 2000-US2430	20000131
		NO 2001-3744	20010731
EP 1148897	A1	EP 2000-905869	20000131
		WO 2000-US2430	20000131
BR 2000007892	A	BR 2000-7892	20000131
		WO 2000-US2430	20000131

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000027483 A Based on WO 200044413
EP 1148897 A1 Based on WO 200044413
BR 2000007892 A Based on WO 200044413

PRIORITY APPLN. INFO: US 2000-493543 20000128; US 1999-118160P 19990201

L8 ANSWER 6 OF 6 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
AN 2000-514778 [46] WPIX
AB WO 200044413 A UPAB: 20000921
NOVELTY - **Regeneration** of **articular cartilage** comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein (BMP).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition for **regeneration** of **articular cartilage** comprising at least one BMP.
USE - For regenerating **articular cartilage** injury or defect. The method can also be used for the treatment of osteoarthritis which will delay or reduce the need for artificial hip replacements.
ADVANTAGE - This new method provides effective repair of articulate cartilage defects and injuries without the need to collect autologous tissue from the patient. Current therapeutic strategies are based on grafting chondral and osteochondral tissues. However, donor tissue is limited and requires surgery at a second site to harvest tissue for implant. As the BMP's can be produced by recombinant DNA technology they are of unlimited supply.
Dwg.0/0
ACCESSION NUMBER: 2000-514778 [46] WPIX
DOC. NO. NON-CPI: N2000-380459
DOC. NO. CPI: C2000-153579
TITLE: **Regeneration** of **articular cartilage** useful for the treatment of osteoarthritis comprises administering to an area in need of **regeneration** at least one purified bone morphogenic protein.
DERWENT CLASS: B04 P34
INVENTOR(S): MORRIS, E; PELUSO, D; ZHANG, R
PATENT ASSIGNEE(S): (GEMY) GENETICS INST INC
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044413	A1	20000803	(200046)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000027483	A	20000818	(200057)		
NO 2001003744	A	20010918	(200169)		
EP 1148897	A1	20011031	(200172)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 2000007892	A	20011030	(200173)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	E
WO 2000044413	A1	WO 2000-US2430	20000131
AU 2000027483	A	AU 2000-27483	20000131
NO 2001003744	A	WO 2000-US2430	20000131
		NO 2001-3744	20010731
EP 1148897	A1	EP 2000-905869	20000131
		WO 2000-US2430	20000131
BR 2000007892	A	BR 2000-7892	20000131
		WO 2000-US2430	20000131

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000027483	A	Based on	WO 200044413
EP 1148897	A1	Based on	WO 200044413
BR 2000007892	A	Based on	WO 200044413

PRIORITY APPLN. INFO: US 2000-493543 20000128; US 1999-118160P 19990201

=> d l9 ti abs ibib tot

L9 ANSWER 1 OF 6 MEDLINE

TI Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis.

AB **Articular cartilage** has a limited ability for repair and/or **regeneration**. Periosteal grafts, having chondrogenic potential, are used clinically and in experimental models to study the repair and **regeneration** of cartilage. **Growth/differentiation factor** 5 (GDF5), recently shown to be involved in chondrogenesis and normal skeletal development, is a bioactive candidate for augmenting the repair of damaged cartilage. In order to investigate the role of GDF5 during periosteal chondrogenesis, the rabbit sequence must be known, as most experimental models involve rabbit tissues. For this purpose, the complete rabbit-specific cDNA sequence of the mature form of GDF5 was determined. Mature rabbit GDF5 was found to be 100% identical to that of human GDF5 at the amino acid level. Using the cDNA sequence, specific primers for PCR were designed. Quantitative RT-PCR, using rabbit-specific primers, showed up-regulation of GDF5 mRNAs early during periosteal chondrogenesis suggesting its potential involvement in this process. The timing and magnitude of this expression was markedly stimulated by TGF-beta 1, which has already been shown to be a potent inducer of periosteal chondrogenesis.

ACCESSION NUMBER: 2001354153 MEDLINE
DOCUMENT NUMBER: 21146954 PubMed ID: 11252805
TITLE: Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis.
AUTHOR: Sanyal A; Sarkar G; Fitzsimmons J S; O'Driscoll S W
CORPORATE SOURCE: Cartilage and Connective Tissue Research Laboratory, Department of Orthopedics, Mayo Clinic, 3-69 Medical Sciences Building, Rochester, MN 55905, USA.
CONTRACT NUMBER: AR43890 (NIAMS)
SOURCE: MOLECULAR BIOTECHNOLOGY, (2000 Nov) 16 (3) 203-10. Journal code: B97; 9423533. ISSN: 1073-6085.
PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

L9 ANSWER 2 OF 6 TOXLIT
TI Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis.
AB **Articular cartilage** has a limited ability for repair and/or **regeneration**. Periosteal grafts, having chondrogenic potential, are used clin. and in exptl. models to study the repair and **regeneration** of cartilage. **Growth/differentiation factor** 5 (GDF5), recently shown to be involved in chondrogenesis and normal skeletal development, is a bioactive candidate for augmenting the repair of damaged cartilage. In order to investigate the role of GDF5 during periosteal chondrogenesis, the rabbit sequence must be known, as most exptl. models involve rabbit tissues. For this purpose, the complete rabbit-specific cDNA sequence of the mature form of GDF5 was detd. Mature rabbit GDF5 was found to be 100% identical to that of human GDF5 at the amino acid level. Using the cDNA sequence, specific primers for PCR were designed. Quant. RT-PCR, using rabbit-specific primers, showed up-regulation of GDF5 mRNAs early during periosteal chondrogenesis suggesting its potential involvement in this process. The timing and magnitude of this expression was markedly stimulated by TGF-.beta.1, which has already been shown to be a potent inducer of periosteal chondrogenesis.
ACCESSION NUMBER: 2000:136476 TOXLIT
DOCUMENT NUMBER: CA-134-305461B
TITLE: Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis.
AUTHOR: Sanyal A; Sarkar G; Fitzsimmons JS; O'Driscoll SW
CORPORATE SOURCE: Department of Orthopedics, Cartilage and Connective Tissue Research Laboratory, Rochester
SOURCE: Mol. Biotechnol., (2000). Vol. 16, No. 3, pp. 203-210. CODEN: MLBOEO. ISSN. 1073-6085.
PUB. COUNTRY: UNITED STATES
DOCUMENT TYPE: Journal; Journal Article
FILE SEGMENT: CA
LANGUAGE: English
OTHER SOURCE: CA 134:305461
ENTRY MONTH: 200105

L9 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2002 BIOSIS
TI Isolation of a cDNA sequence of rabbit GDF5 (Mature Form) and pattern of its mRNA expression during periosteal chondrogenesis.
AB **Articular cartilage** has a limited ability for repair and/or **regeneration**. Periosteal grafts, having chondrogenic potential, are used clinically and in experimental models to study the repair and **regeneration** of cartilage. **Growth/differentiation factor** 5 (GDF5), recently shown to be involved in chondrogenesis and normal skeletal development, is a bioactive candidate for augmenting the repair of damaged cartilage. In order to investigate the role of GDF5 during periosteal chondrogenesis, the rabbit sequence must be known, as most experimental models involve rabbit tissues. For this purpose, the complete rabbit-specific cDNA sequence of the mature form of GDF5 was determined. Mature rabbit GDF5 was found to be 100% identical to that of human GDF5 at the amino acid level. Using the

cDNA sequence, specific primers for PCR were designed. Quantitative RT-PCR, using rabbit-specific primers, showed up-regulation of GDF5 mRNAs early during periosteal chondrogenesis suggesting its potential involvement in this process. The timing and magnitude of this expression was markedly stimulated by TGF-beta1, which has already been shown to be a potent inducer of periosteal chondrogenesis.

ACCESSION NUMBER: 2001:151732 BIOSIS
DOCUMENT NUMBER: PREV200100151732
TITLE: Isolation of a cDNA sequence of rabbit GDF5 (Mature Form) and pattern of its mRNA expression during periosteal chondrogenesis.
AUTHOR(S): Sanyal, Arunik; Sarkar, Gobinda; Fitzsimmons, James S.; O'Driscoll, Shawn W. (1)
CORPORATE SOURCE: (1) Cartilage and Connective Tissue Research Laboratory, Department of Orthopedics, Mayo Clinic, 3-69 Medical Sciences Building, Rochester, MN, 55905 USA
SOURCE: Molecular Biotechnology, (November, 2000) Vol. 16, No. 3, pp. 203-210. print.
ISSN: 1073-6085.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L9 ANSWER 4 OF 6 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
TI Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis.
AB **Articular cartilage** has a limited ability for repair and/or **regeneration**. Periosteal grafts, having chondrogenic potential, are used clinically and in experimental models to study the repair and **regeneration** of cartilage. **Growth/differentiation factor** 5 (GDF5), recently shown to be involved in chondrogenesis and normal skeletal development, is a bioactive candidate for augmenting the repair of damaged cartilage. In order to investigate the role of GDF5 during periosteal chondrogenesis, the rabbit sequence must be known, as most experimental models involve rabbit tissues. For this purpose, the complete rabbit-specific cDNA sequence of the mature form of GDF5 was determined. Mature rabbit GDF5 was found to be 100% identical to that of human GDF5 at the amino acid level. Using the cDNA sequence, specific primers for PCR were designed. Quantitative RT-PCR, using rabbit-specific primers, showed up-regulation of GDF5 mRNAs early during periosteal chondrogenesis suggesting its potential involvement in this process. The timing and magnitude of this expression was markedly stimulated by TGF-.beta.1, which has already been shown to be a potent inducer of periosteal chondrogenesis.
ACCESSION NUMBER: 2001102685 EMBASE
TITLE: Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis.
AUTHOR: Sanyal A.; Sarkar G.; Fitzsimmons J.S.; O'Driscoll S.W.
CORPORATE SOURCE: S.W. O'Driscoll, Cartilage/Connect. Tissue Res. Lab., Department of Orthopedics, Mayo Clinic, Rochester, MN 55905, United States
SOURCE: Applied Biochemistry and Biotechnology - Part B Molecular Biotechnology, (2000) 16/3 (203-210).
Refs: 19
ISSN: 1073-6085 CODEN: MLBOEO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
033 Orthopedic Surgery

LANGUAGE: English
SUMMARY LANGUAGE: English

L9 ANSWER 5 OF 6 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis
AB **Articular cartilage** has a limited ability for repair and/or **regeneration**. Periosteal grafts, having chondrogenic potential, are used clinically and in experimental models to study the repair and **regeneration** of cartilage. **Growth /differentiation factor** 5 (GDF5), recently shown to be involved in chondrogenesis and normal skeletal development, is a bioactive candidate for augmenting the repair of damaged cartilage. In order to investigate the role of GDF5 during periosteal chondrogenesis, the rabbit sequence must be known, as most experimental models involve rabbit tissues. For this purpose, the complete rabbit-specific cDNA sequence of the mature form of GDF5 was determined. Mature rabbit GDF5 was found to be 100% identical to that of human GDF5 at the amino acid level. Using the cDNA sequence, specific primers for PCR were designed. Quantitative RT-PCR, using rabbit-specific primers, showed up-regulation of GDF5 mRNAs early during periosteal chondrogenesis suggesting its potential involvement in this process. The timing and magnitude of this expression was markedly stimulated by TGF-beta1, which has already been shown to be a potent inducer of periosteal chondrogenesis.
ACCESSION NUMBER: 2001:168459 SCISEARCH
THE GENUINE ARTICLE: 402CL
TITLE: Isolation of a cDNA sequence of rabbit GDF5 (mature form) and pattern of its mRNA expression during periosteal chondrogenesis
AUTHOR: Sanyal A (Reprint); Sarkar G; Fitzsimmons J S; O'Driscoll S W
CORPORATE SOURCE: Mayo Clin & Mayo Fdn, Dept Orthoped, Cartilage & Connect Tissue Res Lab, Rochester, MN 55905 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BIOTECHNOLOGY, (NOV 2000) Vol. 16, No. 3, pp. 203-210.
Publisher: HUMANA PRESS INC, 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512 USA.
ISSN: 1073-6085.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L9 ANSWER 6 OF 6 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Cartilage-derived morphogenetic proteins and cartilage morphogenesis
AB Cartilage morphogenesis is a prerequisite for skeletal development and maintenance. The morphogenesis of cartilage determines the shape of bones, and joints including **articular cartilage**, ligaments, and tendon. This article reviews the recent advances in cartilage-derived morphogenetic proteins (CDMPs) and related bone morphogenetic proteins (BMPs). Cartilage-derived morphogenetic proteins (CDMPs) are related to BMPs and are critical for cartilage and joint morphogenesis. Cartilage morphogenesis is a multistep cascade that includes factors for initiation, promotion, and maintenance of cartilage phenotype. The extracellular matrix of cartilage consists of a constellation of macromolecules such as collagens, proteoglycans, and glycoproteins. Morphogens bind to extracellular matrix components and assemble a morphogenetic scaffold. Recent advances in CDMPs may aid in **articular cartilage**

repair and **regeneration**. Microsc. Res. Tech. 43:131-136, 1998.
(C) 1998 Wiley-Liss, Inc.
ACCESSION NUMBER: 1[redacted]:854806 SCISEARCH
THE GENUINE ARTICLE: 135JL
TITLE: Cartilage-derived morphogenetic proteins and cartilage morphogenesis
AUTHOR: Reddi A H (Reprint)
CORPORATE SOURCE: RES BLDG 1, ROOM 2000, 4635 2ND AVE, SACRAMENTO, CA 95817 (Reprint); UNIV CALIF DAVIS, SCH MED, CTR TISSUE REGENERAT & REPAIR, DEPT ORTHOPAED SURG, SACRAMENTO, CA 95817
COUNTRY OF AUTHOR: USA
SOURCE: MICROSCOPY RESEARCH AND TECHNIQUE, (15 OCT 1998) Vol. 43, No. 2, pp. 131-136.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 1059-910X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 73
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> d his

(FILE 'HOME' ENTERED AT 12:03:02 ON 14 JAN 2002)

FILE 'MEDLINE, USPATFULL, WPIDS, WPIX, TOXLIT, JAPIO, JICST-EPLUS, FSTA, FROSTI, BIOBUSINESS, CANCERLIT, DIOGENES, TOXCENTER, BIOSIS, BIOTECHDS, PHAR, CEN, CEABA-VTB, EMBASE, DGENE, SCISEARCH' ENTERED AT 12:05:11 ON 14 JAN 2002

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L1         15310 S BONE MORPHOGENETIC PROTEIN
L2          1060 S ARTICULAR CARTILAGE AND REGENERATION
L3            71 S L2 AND L1
L4            31 S L3 AND METHOD
L5            36 S VGR-2
L6          1675 S GROWTH DIFFERENTIATION FACTOR
L7            18 S BONE FORMATION INDUCING PROTEIN
L8             6 S L2 AND L5
L9             6 S L2 AND L6
L10            0 S L2 AND L7
L11            0 S L8 AND L9
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=> d l7 ti abs ibib tot

L7 ANSWER 1 OF 18 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture.
AN 1994-035064 [04] WPIDS
AB WO 9401557 A UPAB: 19940307
A protein (A) having bone formation-inducing activity, comprising amino acids 1-110 of a sequence given in the specification (BIP) is new. More specifically (A) is the maturation protein (residues 1-110) of a protein of -368-110 amino acids, the BIP precursor protein.
Also claimed are: (1) DNA (I) encoding (A) or analogues; (2) prodn. of (A) comprising transforming a cell with (I) and further comprising expression control sequences, and culturing the transformant; and (3) a pharmaceutical compsn. comprising (A) or active fragments together with pharmaceutically-acceptable carriers.

The dosage of (A) contained in the compsn. varies widely depending on admin. route, type of formulation, kind of disease, age and sex of patient, etc. In general dosage is 0.01-100 mg/day for adult. When the active ingredient is implanted in the bone-loss site in the form of a mixt. with collagen, the mixing ratio of (A) to collagen is 4x10power-6 to 4xpower-10xpower-1 wt.%, more pref. 4x10power-5-4x10power-3 wt.%. The amt. of mixt. to be implanted can be determined by the physician according to the severity of disease.

USE - A certain mRNA encodes a protein having the improved bone formation inducing activity that exists in vertebrate bone. This mRNA may be obtd. from the tissue of a vertebrate (e.g. rat, human) to obtain clones of interest, encoding (A). (A) may be used in compsns. useful for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae, etc. and bone fracture.

Dwg.0/13

ACCESSION NUMBER: 1994-035064 [04] WPIDS
DOC. NO. CPI: C1994-016236
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture.
DERWENT CLASS: B04 D16
INVENTOR(S): FUKUDA, K; HINO, J; KANGAWA, K; KONNO, Y; TAKAO, M; TAKESHITA, N; KESHITA, N
PATENT ASSIGNEE(S): (SUMQ) SUMITOMO METAL IND LTD; (MATS-I) MATSUO H
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9401557	A1	19940120	(199404)*	EN	57
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA KR US					
AU 9345141	A	19940131	(199422)		
JP 06172390	A	19940621	(199429)		23

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9401557	A1	WO 1993-JP952	19930709
AU 9345141	A	AU 1993-45141	19930709
JP 06172390	A	JP 1993-193023	19930709

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9345141	A	Based on	WO 9401557

PRIORITY APPLN. INFO: JP 1992-206996 19920713

L7 ANSWER 2 OF 18 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture.
AN 1994-035064 [04] WPIX
AB WO 9401557 A UPAB: 19940307
A protein (A) having bone formation-inducing activity, comprising amino acids 1-110 of a sequence given in the specification (BIP) is new. More

specifically (A) is the maturation protein (residues 1-110) of a protein of -368-110 amino ds, the BIP precursor protein.

Also claimed : (1) DNA (I) encoding (A) or logues; (2) prodn. of (A) comprising transforming a cell with (I) and further comprising expression control sequences, and culturing the transformant; and (3) a pharmaceutical compsn. comprising (A) or active fragments together with pharmaceutically-acceptable carriers.

The dosage of (A) contained in the compsn. varies widely depending on admin. route, type of formulation, kind of disease, age and sex of patient, etc. In general dosage is 0.01-100 mg/day for adult. When the active ingredient is implanted in the bone-loss site in the form of a mixt. with collagen, the mixing ratio of (A) to collagen is 4x10power-6 to 4xpower-10xpower-1 wt.%, more pref. 4x10power-5-4x10power-3 wt.%. The amt. of mixt. to be implanted can be determined by the physician according to the severity of disease.

USE - A certain mRNA encodes a protein having the improved bone formation inducing activity that exists in vertebrate bone. This mRNA may be obtd. from the tissue of a vertebrate (e.g. rat, human) to obtain clones of interest, encoding (A). (A) may be used in compsns. useful for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae, etc. and bone fracture.

Dwg.0/13

ACCESSION NUMBER: 1994-035064 [04] WPIX
DOC. NO. CPI: C1994-016236
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture.
DERWENT CLASS: B04 D16
INVENTOR(S): FUKUDA, K; HINO, J; KANGAWA, K; KONNO, Y; TAKAO, M; TAKESHITA, N; KESHITA, N
PATENT ASSIGNEE(S): (SUMQ) SUMITOMO METAL IND LTD; (MATS-I) MATSUO H
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9401557	A1	19940120	(199404)*	EN	57
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA KR US					
AU 9345141	A	19940131	(199422)		
JP 06172390	A	19940621	(199429)		23

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9401557	A1	WO 1993-JP952	19930709
AU 9345141	A	AU 1993-45141	19930709
JP 06172390	A	JP 1993-193023	19930709

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9345141	A	Based on	WO 9401557

PRIORITY APPLN. INFO: JP 1992-206996 19920713

L7 ANSWER 3 OF 18 TOXLIT

TI Purification of bone morphogenetic protein from bone tissues with immobilized concar[redacted]alin A.
AB Purifn. of bone mo[redacted]hogenetic protein (**bone formati[redacted] inducing protein**) from e.g. calf bone tissues involves: chromatog. on heparin-Sepharose hydroxyapatite-Ultrogel, Con A-Sepharose 4B and again heparin-Sepharose.
ACCESSION NUMBER: 1993:22624 TOXLIT
DOCUMENT NUMBER: CA-118-053151M
TITLE: Purification of bone morphogenetic protein from bone tissues with immobilized concaravalin A.
AUTHOR: Shiba A; Shiba K; Kino A
SOURCE: (1992). Jpn. Kokai Tokkyo Koho PATENT NO. 92235197 08/24/92
(Shiseido Co., Ltd.).
PUB. COUNTRY: Japan
DOCUMENT TYPE: Patent
FILE SEGMENT: CA
LANGUAGE: Japanese
OTHER SOURCE: CA 118:53151
ENTRY MONTH: 199304

L7 ANSWER 4 OF 18 BIOTECHDS COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein;**
human or rat recombinant osteogenic protein production for use in osteoporosis, alveolar pyorrhae, bone fracture, etc., therapy; DNA sequence
AN 1994-03151 BIOTECHDS
AB A human or rat osteogenic protein (I) of disclosed protein sequence (bases 1-110) is claimed. The following are also claimed: (1) DNA (II) encoding (I) or (I) analogs of disclosed DNA sequence (bases 1,191-1,520 or 87-1,520) and its analogs; (2) a method for producing (I) involving transforming a cell with (II) encoding (I) and expression control sequences and culturing the transformant; (3) a pharmaceutical composition comprising (I) or active fragments and pharmaceutically-acceptable adjuvants; and (4) a pharmaceutical composition containing (I)
or its active fragments for implantation. The pharmaceutical compositions may be used in therapy of bone diseases e.g. osteoporosis, alveolar pyorrhae, etc. and bone fracture. (57pp)
ACCESSION NUMBER: 1994-03151 BIOTECHDS
TITLE: **Bone formation-inducing protein;**
human or rat recombinant osteogenic protein production for
use in osteoporosis, alveolar pyorrhae, bone fracture, etc., therapy; DNA sequence
PATENT ASSIGNEE: Sumitomo-Metal
PATENT INFO: WO 9401557 20 Jan 1994
APPLICATION INFO: WO 1993-JP952 9 Jul 1993
PRIORITY INFO: JP 1992-206996 13 Jul 1992
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1994-035064 [04]

L7 ANSWER 5 OF 18 CEABA-VTB COPYRIGHT 2002 DECHEMA
TI **Bone formation-inducing protein**
AN 1995(07):5516 CEABA-VTB FS B
AB A protein is disclosed which has a high activity for inducing bone formation. A DNA encoding the protein is also disclosed as well as a method for producing the protein and a pharmaceutical comprising the protein as an active ingredient.
FILE SEGMENT B
DOCUMENT NUMBER: CEABA: 1995:9828890
TITLE: **Bone formation-inducing**

protein
AUTHOR: [redacted]Kangawa, Kenji; Hino, Jun; Fukuda, Kenji; Takao Makoto; Takeshite, Norimatsu; [redacted]no Yasuhiko
(Sumitomo
Metal Ind., Ltd., Osaka-shi, Osaka-fu 541, Japan)
SOURCE: PCT Patent Appl. (1994) WO 9401557(Appl. JP 4/206996, Filed 13 Jul 1992)
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

L7 ANSWER 6 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture
AB Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g.
human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAR47586 Protein DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 7 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture
AB Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g.
human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAR47587 Protein DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 8 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture

AB Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g. human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.

ACCESSION NUMBER: AAQ54050 cDNA to mRNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 9 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
AB Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g. human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.

ACCESSION NUMBER: AAQ54052 cDNA to mRNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 10 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
AB The primers given in AAQ54053-54 were used in the amplification of human DNA. A fragment of ca 180 bp (AAQ54051) was obtained and further used as probe to screen a cDNA library of human bone tissue. Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g. human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.

ACCESSION NUMBER: AAQ54051 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p

APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 11 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture
AB The primers given in AAQ54053-54 were used in the amplification of human DNA. A fragment of ca 180 bp (AAQ54051) was obtained and further used as
probe to screen a cDNA library of human bone tissue. Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g. human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAQ54053 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 12 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture
AB The primers given in AAQ54053-54 were used in the amplification of human DNA. A fragment of ca 180 bp (AAQ54051) was obtained and further used as
probe to screen a cDNA library of human bone tissue. Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g. human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAQ54054 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 13 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** -
for therapy of diseases involving osteoporosis, a bone deficiency such as

alveolar pyorrhae etc. and bone fracture
AB The primers given ' AAQ54055-58 were used in the amplification of rat DNA. Protein havi improved bone formation induci activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g.
human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAQ54055 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 14 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture
AB The primers given in AAQ54055-58 were used in the amplification of rat DNA. Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g.
human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAQ54056 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 15 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as
alveolar pyorrhae etc. and bone fracture
AB The primers given in AAQ54055-58 were used in the amplification of rat DNA. Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g.
human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAQ54057 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.

PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 16 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
AB The primers given in AAQ54055-58 were used in the amplification of rat DNA. Protein having improved bone formation inducing-activity has been provided. BIP mRNA may be obtained from the tissue of a vertebrate (e.g. human, rat) and used in recombinant DNA techniques for the prodn. of the protein. The BIP us useful in pharmaceuticals.
ACCESSION NUMBER: AAQ54058 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 17 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
AB The 5' and 3' end of the sense strand overhangs the antisense strand by 4 bases. In order to cleave the BIP maturation protein from the precursor more efficiently, the original process site is replaced by a consensus sequence, e.g. the BMP-2 type or proactivin A type process site (AAQ54059-60).
ACCESSION NUMBER: AAQ54060 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
INVENTOR: Fukuda K; Hino J; Kangawa K; Keshita N; Konno Y; Takao M
PATENT ASSIGNEE: (SUMQ)SUMITOMO METAL IND LTD.
PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]

L7 ANSWER 18 OF 18 DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
TI **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
AB The 5' and 3' end of the sense strand overhangs the antisense strand by 4

bases. In order to cleave the BIP maturation protein from the precursor more efficiently, the original process site is replaced by a consensus sequence, e.g. th[redacted]MP-2 type or proactivin A type[redacted]ocess site (AAQ54059-60).

ACCESSION NUMBER: AAQ54059 DNA DGENE
TITLE: **Bone formation-inducing protein** - for therapy of diseases involving osteoporosis, a bone deficiency such as alveolar pyorrhae etc. and bone fracture
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PATENT INFO: WO 9401557 A 19940120 57p
APPLICATION INFO: WO 1993-JP952 19930709
PRIORITY INFO: JP 1992-206996 19920713
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 1994-035064 [04]